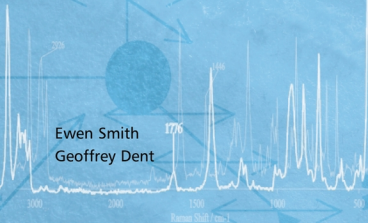


# Modern Raman Spectroscopy

A Practical Approach

Ewen Smith  
Geoffrey Dent



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**Ewen Smith**

*Strathclyde University, Glasgow*

**Geoffrey Dent**

*Intertek ASG and UMIST, Manchester*



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# Preface

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For many years the practice of Raman spectroscopy was confined to experts in dedicated academic or industrial research laboratories. The instruments were large, complicated and the experiments could be quite complex. With advances in modern technology, Raman spectrometers have become small, portable and are regularly used by people who are neither specialist spectroscopists nor analysts. Often instruments are bought for a specific application but eventually the user asks, 'What else can this be used for?'. Whilst much good work continues to be carried on by Raman experts in rolling back the frontiers in advanced techniques, this book is addressed to the more general, modern, application-driven user. Our aim in writing this book is to provide the information necessary to enable new users to understand and apply the technique correctly. This includes descriptions of the many pitfalls that can be encountered. We wish to aid those with a more sustained interest to gain sufficient knowledge and understanding to make full use of the high information content that Raman scattering can afford. With this approach in mind, we have provided in the early chapters enough basic theory to make a practical interpretation of Raman spectra. The theory is dealt with in a little more depth in later chapters where the approach is to describe the main equations used to explain Raman scattering, but concentrating on their meaning and relevance rather than a full mathematical treatment.

With this background the much more detailed world is revealed in which aspects of Raman spectroscopy can provide unique information for a limited number of analytical problems. A full mathematical approach to the theory of Raman spectroscopy is outside the scope of this book. For those who read through to the end, the book will provide a firm grounding, with appropriate references given, from which to approach more in-depth studies of specific aspects of Raman spectroscopy. In writing this book some difficult choices have had to be made particularly around the presentation of the theory. Many current users of Raman spectroscopy have little idea of the underlying modern theory and as a result are at risk of misinterpreting their results. However, whilst a full explanation of theory has to have some mathematics, in the authors' experience many users do not have the time or the background to

understand a fully rigorous mathematical exposition. The non-rigorous mathematical approach is almost essential. We have used as few equations as possible to show how the theory is developed and those are deliberately not in the first chapter. The equations are explained rather than derived so that those with little knowledge of mathematics can understand the physical meaning described. This level of understanding is sufficient for most purposes. Where a more in-depth approach is sought, the explanation would serve as a good starting point. Two theories are often used in Raman spectroscopy – classical theory and quantum theory. A consequence of our approach to the theory is the omission of classical Raman theory altogether. Classical theory does not use quantum mechanics. In the authors' opinion the lack of quantum theory to describe vibrations means that it does not deliver the information required by the average Raman spectroscopist.

One of the practical difficulties faced is in compliance with the IUPAC convention in the description of spectrum scales. Whilst the direction of the wavenumber shift should always be consistent, this is not the practice in most scientific journals or by software writers for instrument companies. Unfortunately the modern practitioner has to view original and reference spectra in differing formats. To illustrate applications we have used the format in which the user is most likely to see a reference spectrum. Equally, where we have used, with permission, literature examples in this book, it would not be possible to change these round to fit the convention. Raman scattering is a shift from an exciting frequency and should be labelled  $\Delta\text{cm}^{-1}$ . However it is common practice to use  $\text{cm}^{-1}$  with the delta implied. Changing labels on previously published examples would not be permitted so for simplicity and consistency we have used the common format. We apologise to the purists who would prefer complete compliance with the IUPAC convention, but we have found that it is not practicable.

It is the authors' hope that those who are just developing or reviving an interest in Raman spectroscopy will very quickly gain a practical understanding from the first two chapters. Furthermore they will be inspired by the elegance and information content of the technique to delve further into the rest of the book, and explore the vast potential of the more sophisticated applications of Raman spectroscopy.

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# Chapter 1

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## Introduction, Basic Theory and Principles

### 1.1 INTRODUCTION

The main spectroscopies employed to detect vibrations in molecules are based on the processes of infrared absorption and Raman scattering. They are widely used to provide information on chemical structures and physical forms, to identify substances from the characteristic spectral patterns ('fingerprinting'), and to determine quantitatively or semi-quantitatively the amount of a substance in a sample. Samples can be examined in a whole range of physical states; for example, as solids, liquids or vapours, in hot or cold states, in bulk, as microscopic particles, or as surface layers. The techniques are very wide ranging and provide solutions to a host of interesting and challenging analytical problems. Raman scattering is less widely used than infrared absorption, largely due to problems with sample degradation and fluorescence. However, recent advances in instrument technology have simplified the equipment and reduced the problems substantially. These advances, together with the ability of Raman spectroscopy to examine aqueous solutions, samples inside glass containers and samples without any preparation, have led to a rapid growth in the application of the technique.

In practice, modern Raman spectroscopy is simple. Variable instrument parameters are few, spectral manipulation is minimal and a simple interpretation of the data may be sufficient. This chapter and Chapter 2 aim to set out the basic principles and experimental methods to give the reader a firm understanding of the basic theory and practical considerations so that the technique



can be applied at the level often required for current applications. However, Raman scattering is an underdeveloped technique, with much important information often not used or recognized. Later chapters will develop the minimum theory required to give a more in-depth understanding of the data obtained and to enable comprehension of some of the many more advanced techniques which have specific advantages for some applications.

### **1.1.1 History**

The phenomenon of inelastic scattering of light was first postulated by Smekal in 1923 [1] and first observed experimentally in 1928 by Raman and Krishnan [2]. Since then, the phenomenon has been referred to as Raman spectroscopy. In the original experiment sunlight was focussed by a telescope onto a sample which was either a purified liquid or a dust-free vapour. A second lens was placed by the sample to collect the scattered radiation. A system of optical filters was used to show the existence of scattered radiation with an altered frequency from the incident light – the basic characteristic of Raman spectroscopy.

## **1.2 BASIC THEORY**

When light interacts with matter, the photons which make up the light may be absorbed or scattered, or may not interact with the material and may pass straight through it. If the energy of an incident photon corresponds to the energy gap between the ground state of a molecule and an excited state, the photon may be absorbed and the molecule promoted to the higher energy excited state. It is this change which is measured in absorption spectroscopy by the detection of the loss of that energy of radiation from the light. However, it is also possible for the photon to interact with the molecule and scatter from it. In this case there is no need for the photon to have an energy which matches the difference between two energy levels of the molecule. The scattered photons can be observed by collecting light at an angle to the incident light beam, and provided there is no absorption from any electronic transitions which have similar energies to that of the incident light, the efficiency increases as the fourth power of the frequency of the incident light.

Scattering is a commonly used technique. For example, it is widely used for measuring particle size and size distribution down to sizes less than 1  $\mu\text{m}$ . One everyday illustration of this is that the sky is blue because the higher energy blue light is scattered from molecules and particles in the atmosphere more efficiently than the lower energy red light. However, the main scattering technique used for molecular identification is Raman scattering.

The process of absorption is used in a wide range of spectroscopic techniques. For example it is used in acoustic spectroscopy where there is a very small energy difference between the ground and excited states and in X-ray absorption spectroscopy where there is a very large difference. In between these extremes are many of the common techniques such as NMR, EPR, infrared absorption, electronic absorption and fluorescence emission, and vacuum ultraviolet (UV) spectroscopy. Figure 1.1 indicates the wavelength ranges of some commonly used types of radiation.

Radiation is often characterized by its wavelength ( $\lambda$ ). However, in spectroscopy, because we are interested in the interaction of radiation with states of the molecule being examined and this being usually discussed in terms of energy, it is often useful to use frequency ( $\nu$ ) or wavenumber ( $\bar{\sigma}$ ) scales, which are linearly related with energy. The relationships between these scales are given below:

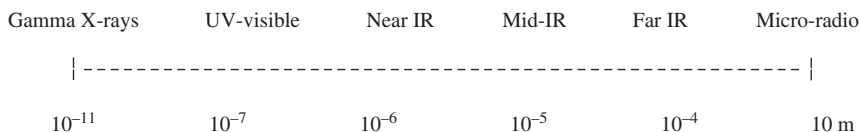
$$\lambda = c/\nu \quad (1.1)$$

$$\nu = \Delta E/h \quad (1.2)$$

$$\bar{\sigma} = \nu/c = 1/\lambda \quad (1.3)$$

It is clear from Equations (1.1)–(1.3) that the energy is proportional to the reciprocal of wavelength and therefore the highest energy region is on the left in Figure 1.1 and the longest wavelength on the right.

The way in which radiation is employed in infrared and Raman spectroscopies is different. In infrared spectroscopy, infrared energy covering a range of frequencies is directed onto the sample. Absorption occurs where the frequency of the incident radiation matches that of a vibration so that the molecule is promoted to a vibrational excited state. The loss of this frequency of radiation from the beam after it passes through the sample is then detected. In contrast, Raman spectroscopy uses a single frequency of radiation to irradiate the sample and it is the radiation scattered from the molecule, one vibrational unit of energy different from the incident beam, which is detected. Thus, unlike infrared absorption, Raman scattering does not require matching of the incident radiation to the energy difference between the ground and excited states. In Raman scattering, the light interacts with the molecule and distorts (polarizes) the cloud of electrons round the nuclei to form a short-lived state

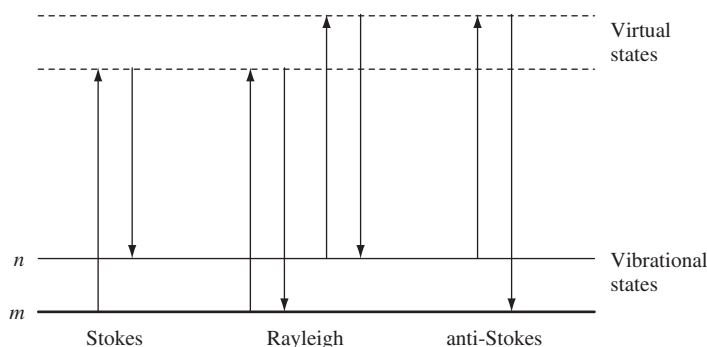


**Figure 1.1.** The electromagnetic spectrum on the wavelength scale in metres.

called a ‘virtual state’, which is discussed in Chapter 3. This state is not stable and the photon is quickly re-radiated.

The energy changes we detect in vibrational spectroscopy are those required to cause nuclear motion. If only electron cloud distortion is involved in scattering, the photons will be scattered with very small frequency changes, as the electrons are comparatively light. This scattering process is regarded as elastic scattering and is the dominant process. For molecules it is called Rayleigh scattering. However, if nuclear motion is induced during the scattering process, energy will be transferred either from the incident photon to the molecule or from the molecule to the scattered photon. In these cases the process is inelastic and the energy of the scattered photon is different from that of the incident photon by one vibrational unit. This is Raman scattering. It is inherently a weak process in that only one in every  $10^6$ – $10^8$  photons which scatter is Raman scattered. In itself this does not make the process insensitive since with modern lasers and microscopes, very high power densities can be delivered to very small samples but it does follow that other processes such as sample degradation and fluorescence can readily occur.

Figure 1.2 shows the basic processes which occur for one vibration. At room temperature, most molecules, but not all, are present in the lowest energy vibrational level. Since the virtual states are not real states of the molecule but are created when the laser interacts with the electrons and causes polarization, the energy of these states is determined by the frequency of the light source used. The Rayleigh process will be the most intense process since most photons scatter this way. It does not involve any energy change and consequently the light returns to the same energy state. The Raman scattering process from the ground vibrational state  $m$  leads to absorption of energy by the molecule and its promotion to a higher energy excited vibrational state ( $n$ ). This is called Stokes

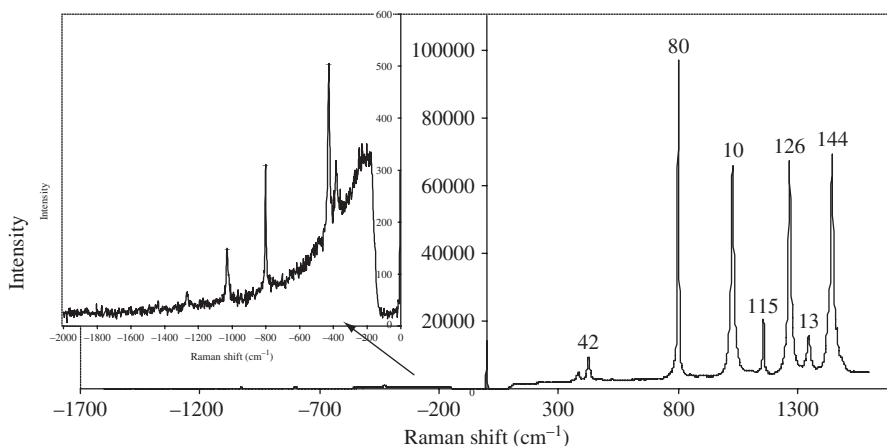


**Figure 1.2.** Diagram of the Rayleigh and Raman scattering processes. The lowest energy vibrational state  $m$  is shown at the foot with states of increasing energy above it. Both the low energy (upward arrows) and the scattered energy (downward arrows) have much larger energies than the energy of a vibration.

scattering. However, due to thermal energy, some molecules may be present in an excited state such as  $n$  in Figure 1.2. Scattering from these states to the ground state  $m$  is called anti-Stokes scattering and involves transfer of energy to the scattered photon. The relative intensities of the two processes depend on the population of the various states of the molecule. The populations can be worked out from the Boltzmann equation (Chapter 3) but at room temperature, the number of molecules expected to be in an excited vibrational state other than any really low-energy ones will be small.

Thus, compared to Stokes scattering, anti-Stokes scattering will be weak and will become weaker as the frequency of the vibration increases, due to decreased population of the excited vibrational states. Further, anti-Stokes scattering will increase relative to Stokes scattering as the temperature rises. Figure 1.3 shows a typical spectrum of Stokes and anti-Stokes scattering from cyclohexane separated by the intense Rayleigh scattering which should be off-scale close to the point where there is no energy shift. However there is practically no signal close to the frequency of the exciting line along the  $x$ -axis. This is because filters in front of the spectrometer remove almost all light within about  $200\text{ cm}^{-1}$  of the exciting line. Some breakthrough of the laser light can be seen where there is no energy shift at all.

Usually, Raman scattering is recorded only on the low-energy side to give Stokes scattering but occasionally anti-Stokes scattering is preferred. For example, where there is fluorescence interference, this will occur at a lower energy than the excitation frequency and consequently anti-Stokes scattering can be used to avoid interference. The difference in intensities of Raman bands in Stokes and anti-Stokes scattering can also be used to measure temperature.



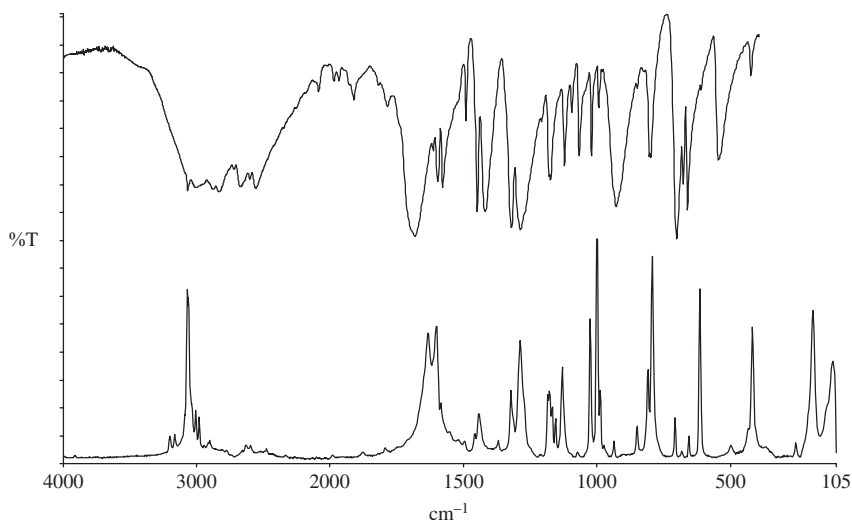
**Figure 1.3.** Stokes and anti-Stokes scattering for cyclohexane. To show the weak anti-Stokes spectrum, the  $y$ -axis has been extended in the inset.

Figure 1.2 illustrates one key difference between infrared absorption and Raman scattering. As described above, infrared absorption would involve direct excitation of the molecule from state  $m$  to state  $n$  by a photon of exactly the energy difference between them. In contrast, Raman scattering uses much higher energy radiation and measures the difference in energy between  $n$  and  $m$  by subtracting the energy of the scattered photon from that of the incident beam (the two vertical arrows in each case).

The cyclohexane spectrum in Figure 1.3 shows that there is more than one vibration which gives effective Raman scattering (i.e. is Raman active); the nature of these vibrations will be discussed in Section 1.3. However, there is a basic selection rule which is required to understand this pattern. Intense Raman scattering occurs from vibrations which cause a change in the polarizability of the electron cloud round the molecule. Usually, symmetric vibrations cause the largest changes and give the greatest scattering. This contrasts with infrared absorption where the most intense absorption is caused by a change in dipole and hence asymmetric vibrations which cause this are the most intense. As will be seen later, not all vibrations of a molecule need, or in some cases can, be both infrared and Raman active and the two techniques usually give quite different intensity patterns. As a result the two are often complementary and, used together, give a better view of the vibrational structure of a molecule.

One specific class of molecule provides an additional selection rule. In a centrosymmetric molecule, no band can be active in both Raman scattering and infrared absorption. This is sometimes called the mutual exclusion rule. In a centrosymmetric molecule, reflection of any point through the centre will reach an identical point on the other side ( $\text{C}_2\text{H}_4$  is centrosymmetric,  $\text{CH}_4$  is not). This distinction is useful particularly for small molecules where a comparison of the spectra obtained from infrared absorption and Raman scattering can be used to differentiate *cis* and *trans* forms of a molecule in molecules such as a simple azo dye or a transition metal complex.

Figure 1.4 shows a comparison of the infrared and Raman spectra for benzoic acid. The  $x$ -axis is given in wavenumbers for which the unit is  $\text{cm}^{-1}$ . Wavenumbers are not recommended SI units but the practice of spectroscopy is universally carried out using these and this is unlikely to change. For infrared absorption each peak represents an energy of radiation absorbed by the molecule. The  $y$ -axis gives the amount of the light absorbed and is usually shown with the maximum absorbance as the lowest point on the trace. Raman scattering is presented only as the Stokes spectrum and is given as a shift in energy from the energy of the laser beam. This is obtained by subtracting the scattered energy from the laser energy. In this way the difference in energy corresponding to the ground and excited vibrational states ( $n$  and  $m$  in Figure 1.2) is obtained. This energy difference is what is measured directly by infrared. The scattering is measured as light detected by the spectrometer and the maximum amount of light detected is the highest point on the trace.



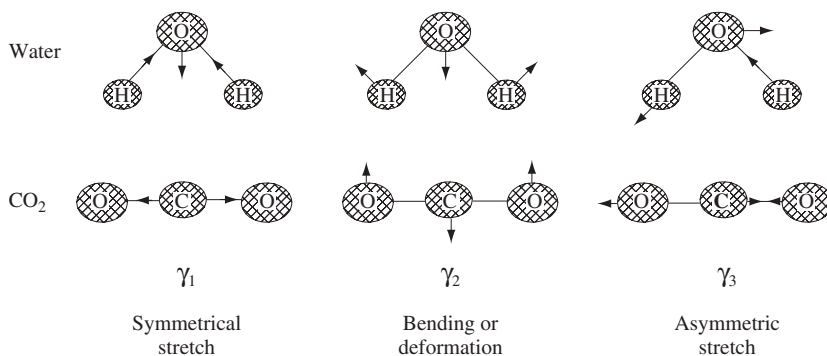
**Figure 1.4.** Infrared and Raman spectra of benzoic acid. The top trace is infrared absorption given in % transmission (%T) so that the lower the transmission value the greater the absorption. The lower trace is Raman scattering and the higher the peak the greater the scattering.

Strictly speaking, Raman scattering should be expressed as a shift in energy from that of the exciting radiation and should be referred to as  $\Delta \text{cm}^{-1}$  but it is often expressed simply as  $\text{cm}^{-1}$ . This practice is followed in this book for simplicity. Although different energy ranges are possible, the information of interest to most users is in the  $3600\text{--}400\text{cm}^{-1}$  (2.8–12 micron) range in infrared spectroscopy and down to  $200\text{cm}^{-1}$  in Raman spectroscopy since this includes most modes which are characteristic of a molecule. In some applications, much larger or smaller energy changes are studied and modern Raman equipment can cope with much wider ranges. One specific advantage of Raman scattering is that shifts from the laser line of  $50\text{cm}^{-1}$  or lower can easily be recorded with the correct equipment. Many modern machines for reasons of cost and simplicity are not configured in a suitable way to measure shifts below  $100\text{--}200\text{cm}^{-1}$ . The intensities of the bands in the Raman spectrum are dependent on the nature of the vibration being studied and on instrumentation and sampling factors. Modern instruments should be calibrated to remove the instrument factors but this is not always the case; these factors are dealt with in the next chapter. Sampling has a large effect on the absolute intensities, bandwidths observed and band positions. Again these will be dealt with later. This chapter will concentrate on the effect on Raman scattering of the set of vibrations present in a molecule and set out a step-by-step approach to interpretation based on simple selection rules.

### 1.3 MOLECULAR VIBRATIONS

Provided that there is no change in electronic energy, for example, by the absorption of a photon and the promotion of an electron to an excited electronic state, the energy of a molecule can be divided into a number of different parts or ‘degrees of freedom’. Three of these degrees of freedom are taken up to describe the translation of the molecule in space and three to describe rotational movement except for linear molecules where only two types of rotation are possible. Thus, if  $N$  is the number of atoms in a molecule, the number of vibrational degrees of freedom and therefore the number of vibrations possible is  $3N - 6$  for all molecules except linear ones where it is  $3N - 5$ . For a diatomic molecule, this means there will be only one vibration. In a molecule such as oxygen, this is a simple stretch of the O–O bond. This will change the polarizability of the molecule but will not induce any dipole change since there is no dipole in the molecule and the vibration is symmetric about the centre. Thus the selection rules already discussed would predict, and it is true, that oxygen gas will give a band in the Raman spectrum and no band in the infrared spectrum. However in a molecule such as nitric oxide, NO, there will be only one band but, since there is both a dipole change and a polarizability change, it will appear in both the infrared and Raman spectrum.

A triatomic molecule will have three modes of vibration. They are a symmetrical stretch, a bending or deformation mode and an asymmetrical stretch as shown in Figure 1.5. The very different water ( $\text{H}_2\text{O}$ ) and carbon dioxide ( $\text{CO}_2$ ) molecules clearly demonstrate these vibrations. These diagrams use ‘spring and ball’ models. The spring represents the bond or bonds between the atoms. The stronger the bond the higher the frequency. The balls represent the atoms and the heavier they are the lower the frequency. The expression which relates the mass of the atoms and the bond strength to the vibrational frequency is Hooke’s



**Figure 1.5.** Spring and ball model – three modes of vibration for  $\text{H}_2\text{O}$  and  $\text{CO}_2$ .

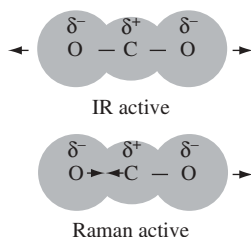
law which is dealt with in Chapter 3, but for the present, it is clear that strong bonds and light atoms will give higher frequencies of vibration and heavy atoms and weak bonds will give lower ones.

This simple model is widely used to interpret vibrational spectra. However, the molecule actually exists as a three-dimensional structure with a pattern of varying electron density covering the whole molecule. A simple depiction of this for carbon dioxide is shown in Figure 1.6. If either molecule vibrates, the electron cloud will alter as the positive nuclei change position and depending on the nature of the change, this can cause a change of dipole moment or polarization. In these triatomic molecules, the symmetrical stretch causes large polarization changes and hence strong Raman scattering with weak or no dipole change and hence weak or no infrared absorption. The deformation mode causes a dipole change but little polarization change and hence strong infrared absorption and weak or non-existent Raman scattering.

As an example of this, Figure 1.7 illustrates the vibrations possible for carbon disulphide along with the corresponding infrared absorption and Raman scattering spectra.

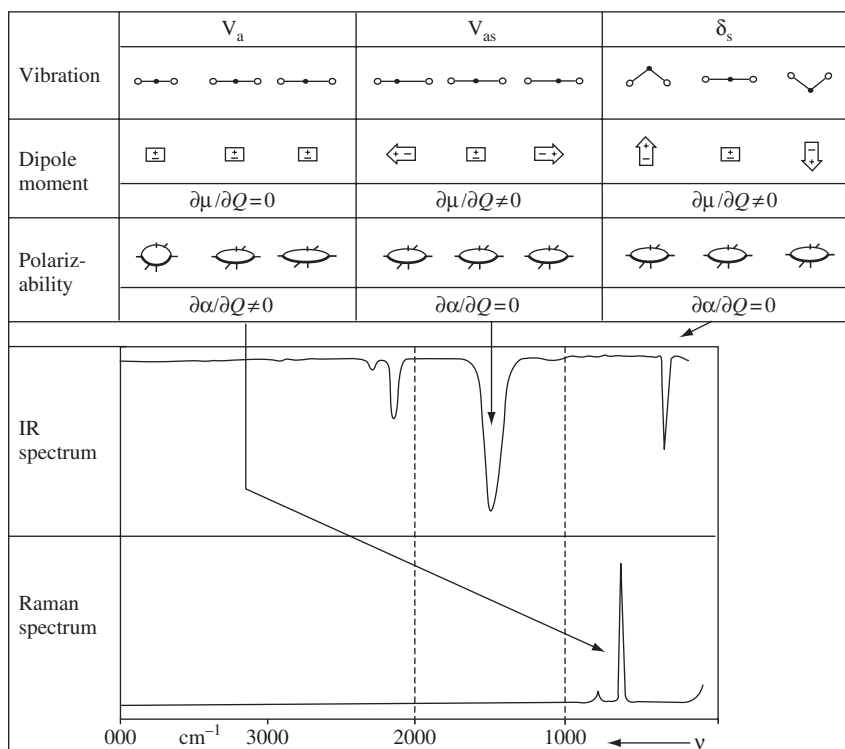
Although this type of analysis is suitable for small molecules, it is more difficult to apply in a more complex molecule. Figure 1.8 shows one vibration from a dye in which a large number of atoms are involved. This is obtained from a theoretical calculation using density functional theory (DFT) which is discussed briefly later. It probably gives a depiction of the vibration which is close to the truth. However, even if it were possible to calculate the spectrum of every molecule quickly in the laboratory, which at present it is not, this type of diagram is only of limited utility to the spectroscopist. A comparison between molecules of similar type is difficult unless a full calculation is available for them all and each subtle change in the nuclear displacements is drawn out or accurately described for each one. This limits the ability to compare large numbers of molecules or to understand the nature of vibrations in molecules for which there is no calculation.

The usual approach to describing vibrations is to simplify the problem and break the displacements down into a number of characteristic features, which



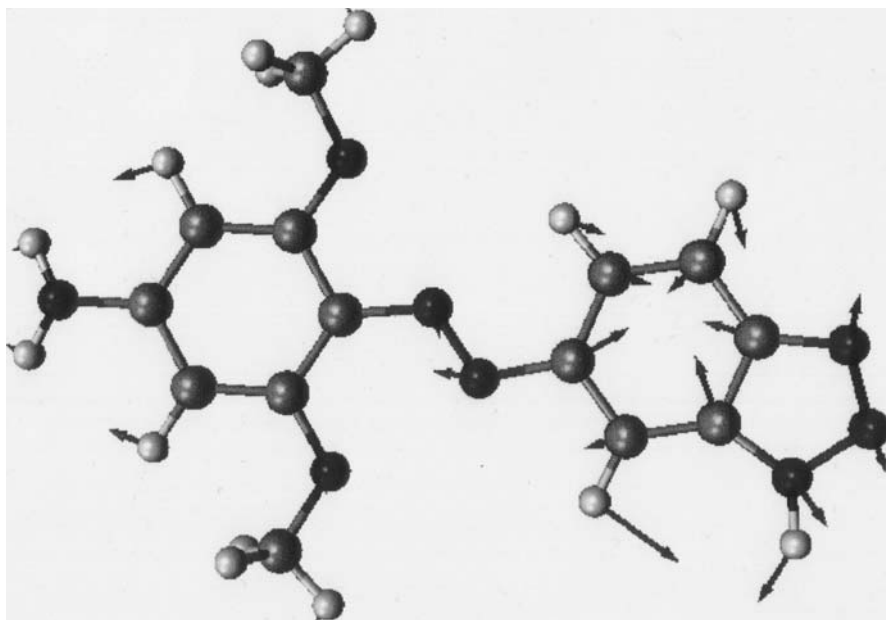
**Figure 1.6.** Electron cloud model of water and carbon dioxide showing an IR and a Raman active vibrations.





**Figure 1.7.** Dipole and polarization changes in carbon disulphide, with resultant infrared and Raman spectra. (Reprinted from A. Fadini and F.-M. Schnepel, *Vibrational Spectroscopy: Methods and Applications*, Ellis Horwood Ltd, Chichester, 1989.)

can relate to more than one molecule. In the vibration in Figure 1.8 which comes from a calculation to predict the energies of vibrations each azo dye, the biggest displacements of the heavier atoms is on one of the ring systems. The vibration would almost certainly be labelled vaguely as a 'ring stretch'. In another vibration not shown the situation was much simpler. Large displacements were found on the two nitrogen atoms which form the azo bond between the rings, and the direction indicated bond lengthening and contracting during the vibrational cycle. Thus this vibration is called the azo stretch, and there is a change in polarizability just as there was for oxygen; so it should be a Raman-active vibration. We can search for these vibrations in the actual spectrum and hopefully match a peak to the vibration. This is called assigning the vibration. Thus, it is possible to describe a vibration in a few helpful words. In some cases this is fairly accurate as for the azo stretch, but in some cases, the description is not adequate to describe the actual movement. However, common bands can be assigned and reasonably described in many molecules.

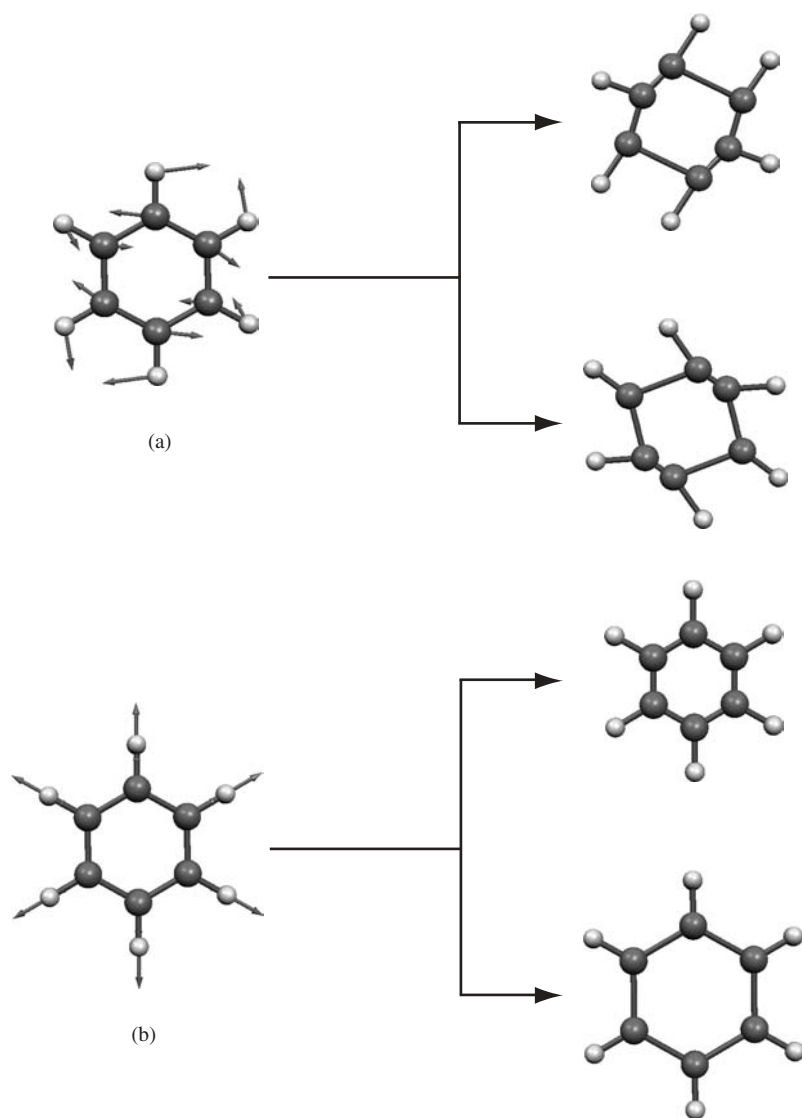


**Figure 1.8.** A displacement diagram for a vibration at about  $1200\text{ cm}^{-1}$  in a dye indicating the involvement of a number of atoms. The arrows show the direction of the displacement. Since the equilibrium position of the atoms is shown, during a complete vibration the arrows will reverse in direction.

### 1.3.1 Group Vibrations

To assign vibrations to spectral peaks it is necessary to realize that two or more bonds which are close together in a molecule and are of similar energies can interact and it is the vibration of the group of atoms linked by these bonds which is observed in the spectrum. For example, the  $\text{CH}_2$  group is said to have a symmetric and an anti-symmetric stretch rather than two separate CH stretches (Figure 1.9). It follows from this and from the geometry of the molecule that different types of vibrations are possible for different groups. Selected examples of a few of these for  $\text{CH}_3$  and  $\text{C}_6\text{H}_6$  are shown in Figure 1.9.

In contrast, where there is a large difference in energy between the vibrations in different bonds or if the atoms are well separated in the molecule, they can be treated separately. Thus, for  $\text{CH}_3\text{Br}$ , the C–H bonds in  $\text{CH}_3$  must be treated as a group but the C–Br vibration is treated separately. In Figure 1.9, the selected vibrations of benzene are shown in two different ways. Firstly they are shown with the molecule in the equilibrium position with arrows showing the direction of the vibrational displacement. To illustrate what this means, they are also shown with the vibration at the extremes of the vibrational movement. To show



**Figure 1.9.** Selected displacement diagrams for benzene and for CH<sub>3</sub> in CH<sub>3</sub>Br. (a) A quadrant stretch for benzene at about  $1600\text{ cm}^{-1}$ . (b) The symmetric breathing mode at just above  $1000\text{ cm}^{-1}$ . (c and d) Two C–H vibrations at about  $3000\text{ cm}^{-1}$ . (e) The symmetric stretch of CH<sub>3</sub> in CH<sub>3</sub>Br at above  $3000\text{ cm}^{-1}$ . (f) An asymmetric stretch at above  $3000\text{ cm}^{-1}$ . (g) A CH bend at about  $1450\text{--}1500\text{ cm}^{-1}$ . (h) A low frequency mode at below  $600\text{ cm}^{-1}$ .

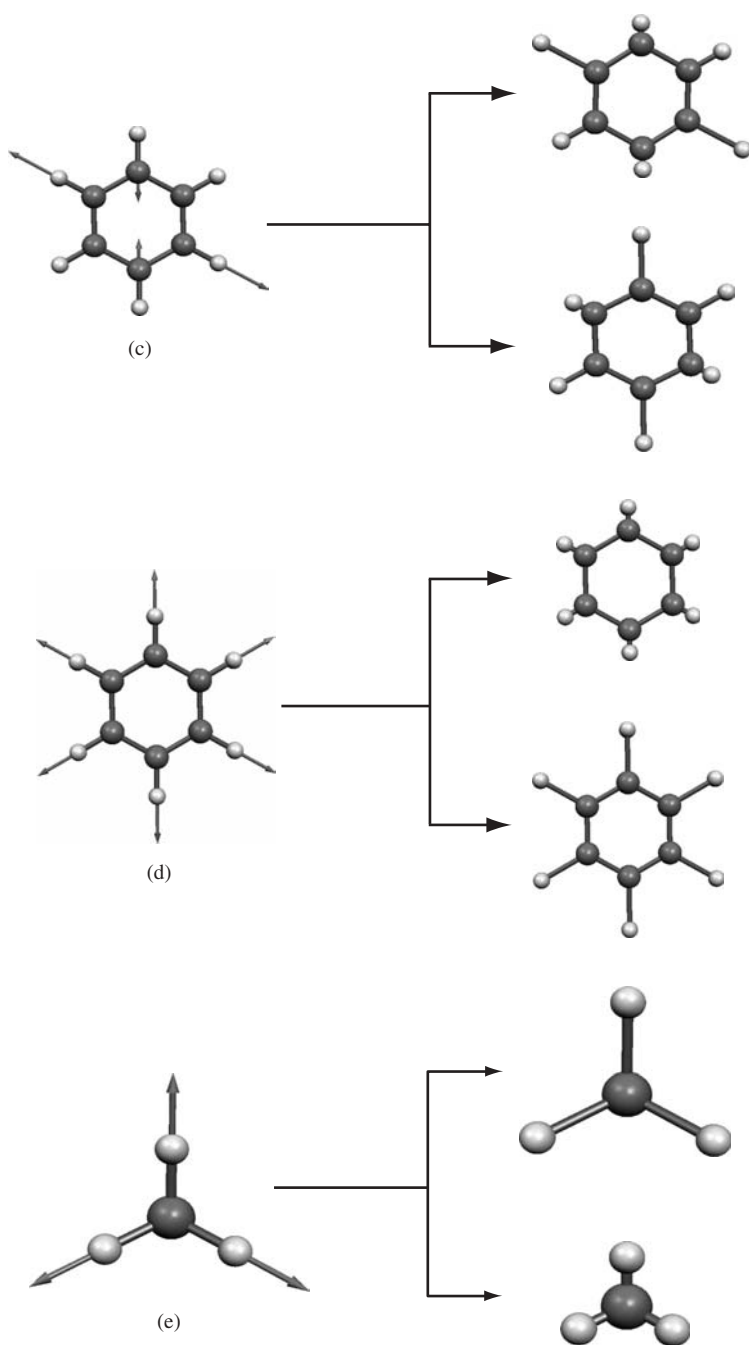
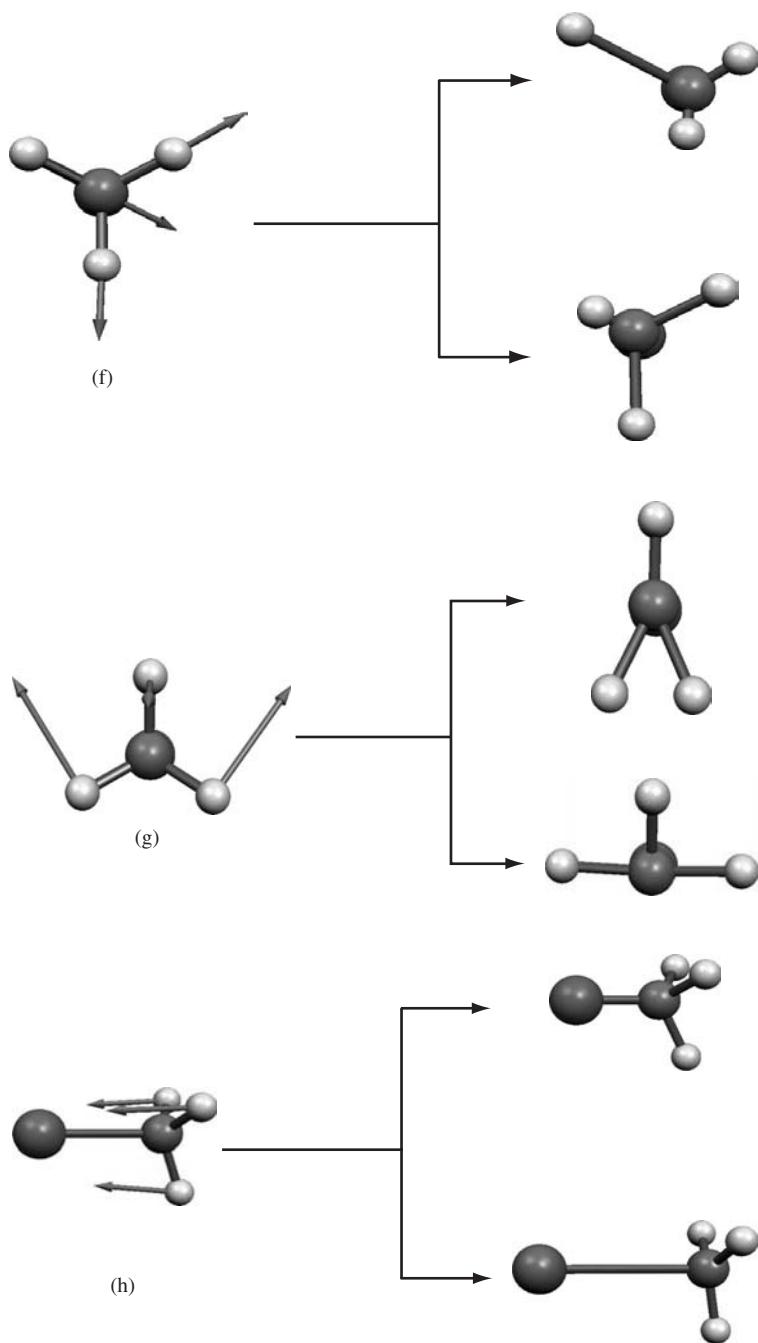


Figure 1.9. Continued.

**Figure 1.9.** Continued.

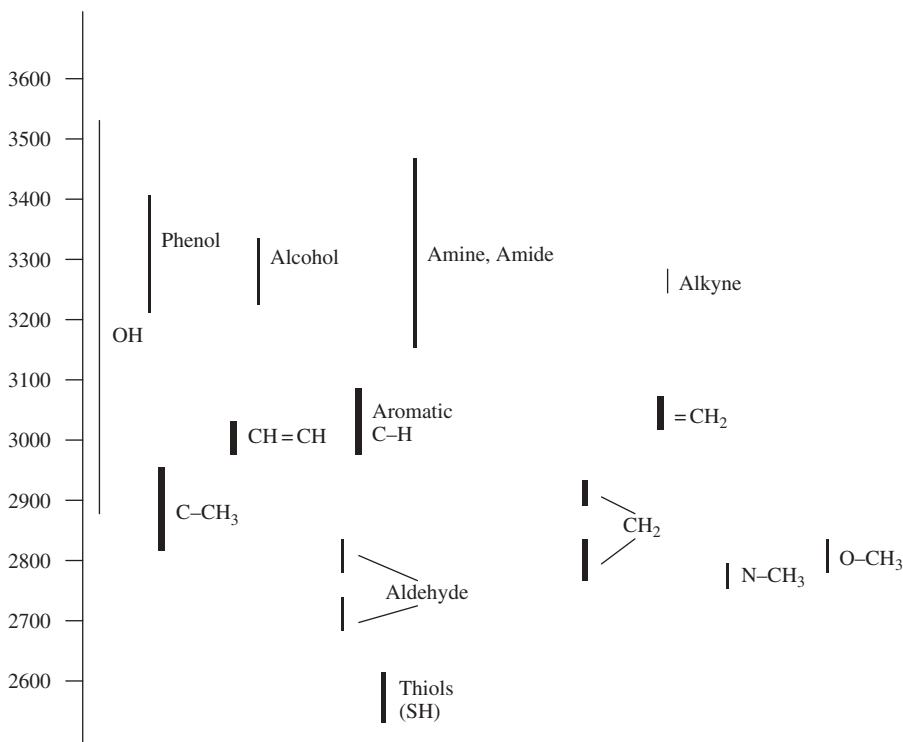
the selected  $\text{CH}_3$  group vibrations, the molecule is completed using a bromine. As discussed, the  $\text{C}-\text{Br}$  bond vibrates at a much lower frequency and does not interact appreciably with the high  $\text{CH}_3$  displacements shown.

### 1.3.2 An Approach to Interpretation

It is possible to give energy ranges in which the characteristic frequencies of the most common groups which are strong in either infrared or Raman scattering can occur. The relative intensities of specific peaks help to confirm that the correct vibration has been picked out.

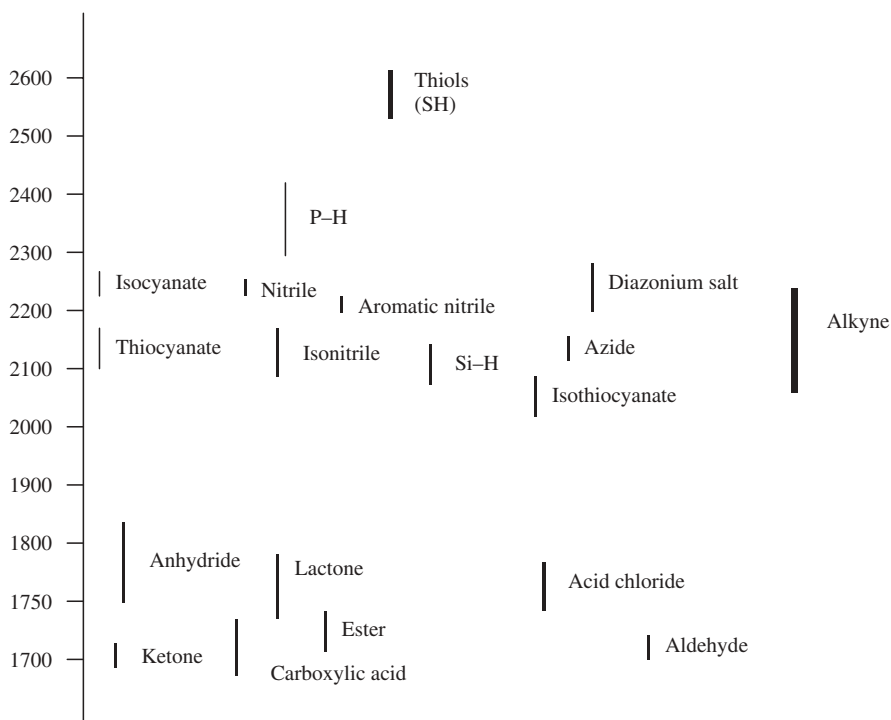
For example, carbonyl groups  $>\text{C}=\text{O}$  which are both asymmetric and ionic will have a dipole moment which will change when the group stretches in a manner analogous to oxygen. They have strong bands in the infrared spectrum

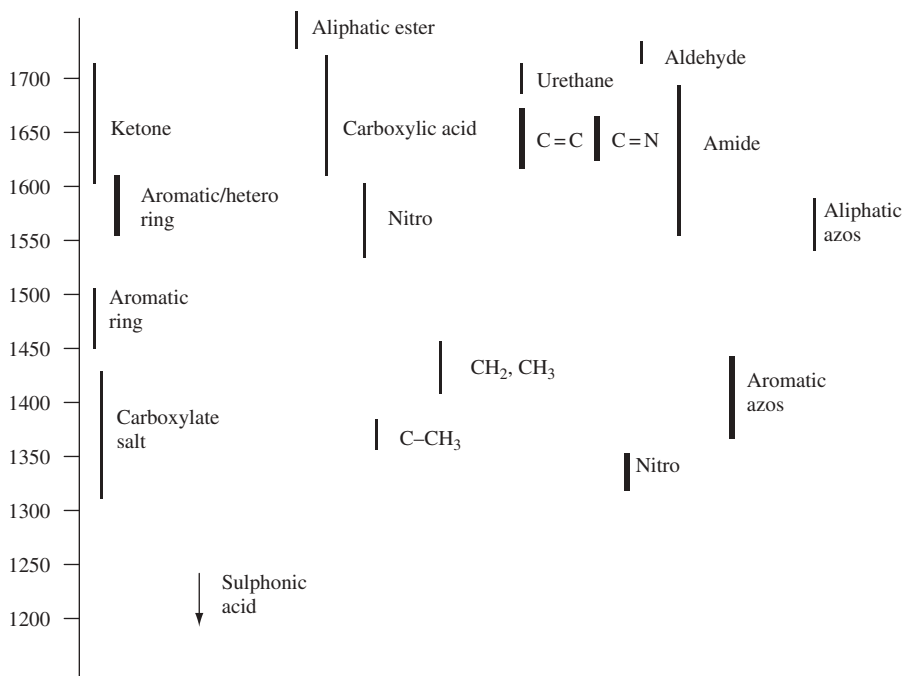
**Table 1.1.** Single vibration and group frequencies and possible intensities of peaks commonly identified in Raman scattering. The length of the vertical line represents the wavenumber range in  $\text{cm}^{-1}$  in which each type of vibration is normally found and the line thickness gives an indication of intensity with thick lines being the most intense.



but are weaker in the Raman spectrum. They are usually present at  $\sim 1700\text{ cm}^{-1}$ . Symmetrical groups such as unsaturated bonds ( $-\text{C}=\text{C}-$ ) and disulphide bonds ( $-\text{S}-\text{S}-$ ) are weak infrared absorbers, but strong Raman scatterers. The stretching modes for these vibrations are  $\sim 1640$  and  $500\text{ cm}^{-1}$  respectively. There are many more examples. It is the combination of the knowledge of approximate energy and likely relative intensity of particular vibrations which form the basis of the assignment mode used by most spectroscopists. For example, the  $4000\text{--}2500\text{ cm}^{-1}$  is the region where single bonds ( $\text{X}-\text{H}$ ) absorb. The  $2500\text{--}2000\text{ cm}^{-1}$  is referred to as the multiple bond ( $-\text{N}=\text{C}=\text{O}$ ) region. The  $2000\text{--}1500\text{ cm}^{-1}$  region is where double bonds ( $-\text{C}=\text{O}$ ,  $-\text{C}=\text{N}$ ,  $-\text{C}=\text{C}-$ ) occur. Below  $1500\text{ cm}^{-1}$ , some groups, e.g. nitro ( $\text{O}=\text{N}=\text{O}$ ) do have specific bands but many molecules have complex patterns of Carbon–Carbon and Carbon–Nitrogen vibrations. The region is generally referred to as the Fingerprint region. Significant bands below  $650\text{ cm}^{-1}$  usually arise from inorganic groups, metal-organic groups or lattice vibrations. Tables 1.1–1.5 show the frequency ranges of

**Table 1.2.** Single vibration and group frequencies and an indication of possible intensities of peaks commonly identified in Raman scattering



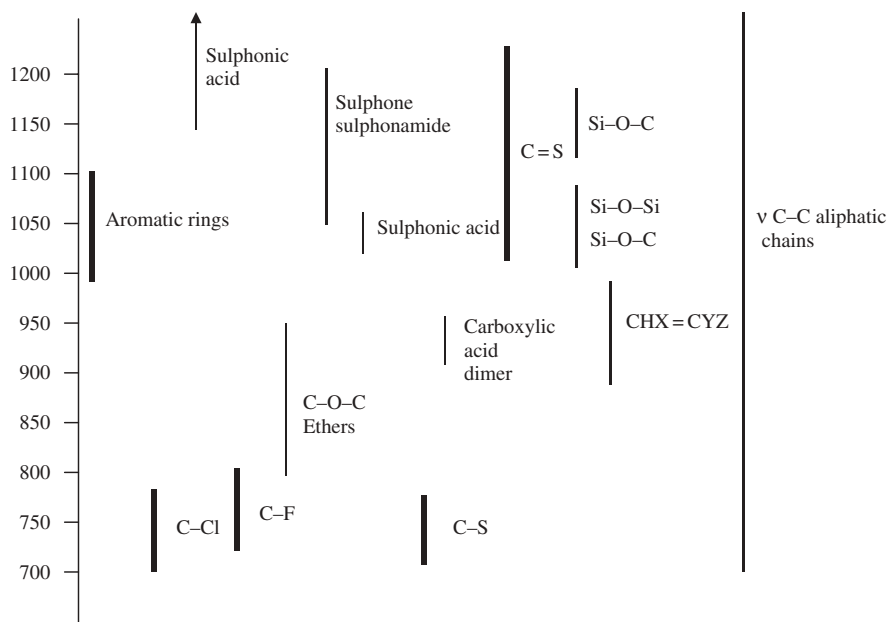
**Table 1.3.** Single vibration and group frequencies and an indication of possible intensities of peaks commonly identified in Raman scattering

many of the vibrations which give rise to strong bands in either Raman or infrared spectroscopy. The ranges are approximate for the groups in most structures but some groups in unusual structures may give bands outside these ranges. The thickness of the line indicates relative strength. These tables enable a beginning to be made on the assignment of specific bands. A more difficult problem is in estimating the relative intensities of the bands. Earlier in this chapter, we showed that there are reasons why in some circumstances bands which are strong in the infrared spectrum are not strong in the Raman spectrum. However, this cannot be taken as an absolute rule although it is the normal behaviour. Thus, the bands that we would expect to be strong in Raman scattering are the more symmetric bands in the spectrum.

This approach is often used in vibrational spectroscopy. However, to assign specific peaks in the spectrum to specific vibrations, modern laboratories use libraries in which complete spectra are stored electronically. Most spectrometers have software to obtain a computer-generated analysis of the similarities and differences with standards so that specific substances can be identified positively and easily. In other areas, the initial assignment is confirmed by

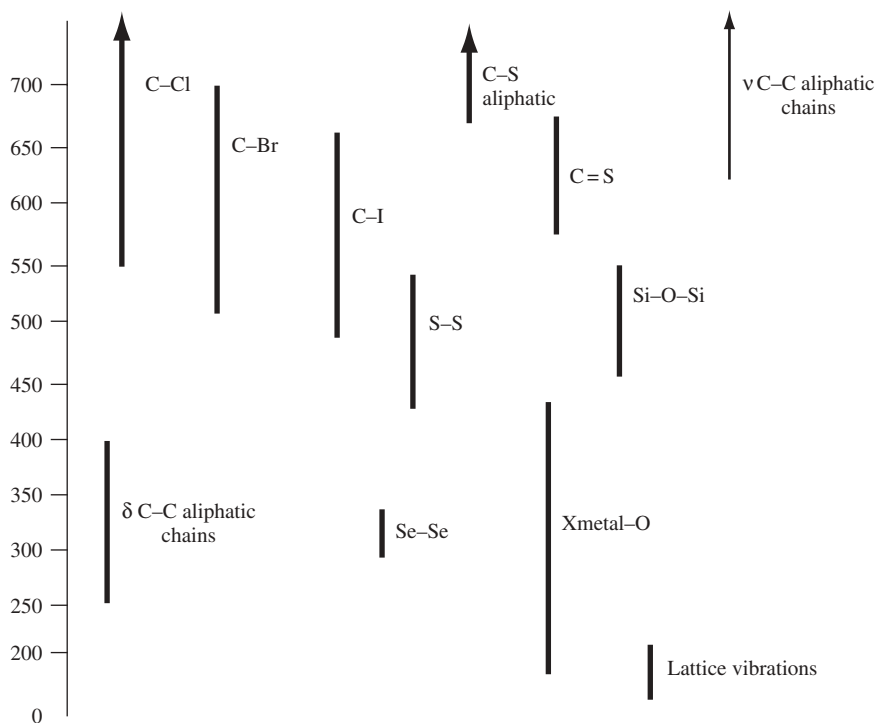


**Table 1.4.** Single vibration and group frequencies and an indication of possible intensities of peaks commonly identified in Raman scattering



DFT calculations, where the great advantages are a more accurate assessment of the nature of the vibrations and hence of molecular structure.

Predicting the principal infrared absorption bands for small molecules is relatively simple as shown above, but for large molecules, the number of bands possible is very large. Fortunately, many of these bands overlap and what is observed at room temperature are broad envelopes with recognizable shapes in some energy regions and sharp bands due to specific bonds such as  $\text{-C=O}$  in some others. Since some vibrations arise from groups of atoms such as the atoms in a carbon chain or from rings linked by bonds of approximately the same energy, the number of peaks and their energies are linked to the overall shape of the molecule. These are called fingerprint bands and the pattern of these bands can help identify a specific molecule *in situ* in a sample. However, for more complex systems, much time can be spent in the assignment of these bands to the bending, stretching or deformation modes but unless the molecule studied is one of a well-understood set such as an alkane chain of a specific length, this more in-depth analysis does not provide much additional help in the majority of first attempts to identify specific materials from the spectrum.

**Table 1.5.** Single vibration and group frequencies and an indication of possible intensities of peaks commonly identified in Raman scattering

Raman spectra are usually somewhat simpler. The most environmentally sensitive bands, e.g. OH and NH, are broad and weak and the backbone structural bands are strong and sharp. The extent of this difference can be illustrated from the fact that water can be used as a solvent to obtain the Raman spectra of organic molecules. This indicates the relative strength of bands in the organic molecule compared to the weakness of hydrogen bonded species such as the OH bands in water. It is this greater selectivity which leads to the simplicity of Raman spectra compared to infrared spectra. Thus, the Raman spectra of quite large molecules show clear bands. In Figure 1.4 the infrared spectrum is complex and has a strong band just above  $1600\text{ cm}^{-1}$  from the carbonyl group due to the C=O vibration. The strong bands in the Raman spectrum are largely due to the aromatic group. The band at  $2900\text{ cm}^{-1}$  due to the  $\text{CH}_2$  group is hidden under the strong OH bands in the infrared spectrum but can be clearly seen in the Raman spectrum.

The above information makes it possible to start assigning and interpreting Raman spectra. If possible it is always good to run an infrared spectrum for

comparison. The phrase ‘interpretation of Raman spectra’ is used in many different ways. The spectrum of a molecule can be the subject of a full mathematical interpretation in which every band is carefully assigned or of a cursory look to produce the interpretation ‘Yes that is toluene’. However, to be able to carry out a complete, correct and relevant interpretation, the total Raman experiment must be considered. Raman spectroscopists have to make a number of choices in deciding how to examine a sample and the type of answer required may ultimately determine these choices. The simplicity and flexibility of Raman scattering are considerable advantages but if care is not taken in making the correct choices, poor or spurious results can be obtained. Chapter 2 describes the choices and provides the background information to enable the recording and interpretation of Raman scattering in a reliable and secure manner.

## 1.4 SUMMARY

In this chapter we have attempted to introduce the reader to the basic principles of Raman spectroscopy without going into the theory and details of practice too deeply, with a view to encouraging further interest. Chapter 2 outlines the practical choices to be made in carrying out the Raman experiment in full. Later chapters give the theoretical background required for full analysis of spectra, a guide to ways in which Raman spectroscopy has been successfully employed, and lead to the more sophisticated but less common techniques available to the Raman spectroscopist.

## REFERENCES

1. A. Smekal, *Naturwissenschaften*, **43**, 873 (1923).
2. C.V. Raman and K.S. Krishnan, *Nature*, **121**, 501 (1928).

## BIBLIOGRAPHY

We have provided a general bibliography. Listed here are a number of publications which the authors have found useful for reference, for theoretical aspects of the spectroscopy and for aids in interpretation.

- J.R. Ferraro and K. Nakamoto, *Introductory Raman Spectroscopy*, Academic Press, San Diego, 1994.
- P. Hendra, C. Jones and G. Warnes, *FT Raman Spectroscopy*, Ellis Horwood Ltd, Chichester, 1991.
- A. Fadini and F.-M. Schnepel, *Vibrational Spectroscopy: Methods and Applications*, Ellis Horwood Ltd, Chichester, 1989.

- N.B. Colthrup, L.H. Daly and S.E. Wiberley, *Introduction to Infrared and Raman Spectroscopy*. 3rd Edition, Academic Press, San Diego, 1990.
- D. Lin-Vien, N.B. Colthrup, W.G. Fateley and J.G. Grasselli, *The Handbook of Infrared and Raman Characteristic Frequencies of Organic Molecules*, John Wiley & Sons, New York, 1991.
- I.A. Degen, *Tables of Characteristic Group frequencies for the Interpretation of Infrared and Raman Spectra*, Acolyte Publications, Harrow, UK, 1997.
- D.M. Adams, *Metal – Ligands and Related Vibrations*, Edward Arnold Ltd, London, 1967.



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## Chapter 2

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# **The Raman Experiment – Raman Instrumentation, Sample Presentation, Data Handling and Practical Aspects of Interpretation**

### **2.1 INTRODUCTION**

The Raman spectroscopist has to make a number of choices in deciding how to examine a sample and the choices made are ultimately determined by the availability of equipment and by the type of answer required. Should the excitation source be in the UV, visible or near-infrared (NIR) frequency region? Should the detection system consist of a dispersive monochromator with a charge coupled device (CCD) detector or an Fourier transform (FT) interferometer with an indium gallium arsenide (InGaAs) detector? Are suitable accessories available to allow the sample to be studied efficiently? How should the sample be presented to the instrument and how can photodegradation and fluorescence be avoided? How do these choices affect the answer? This chapter describes the common types of spectrometer which are used, the accessories available for these instruments, the way in which the sample is presented to the instrument and the way to use data manipulation effectively. The intention is to give guidance in the thought processes required to answer the above questions and others which are essential for a Raman determination to be carried out with confidence.

## 2.2 CHOICE OF INSTRUMENT

In Chapter 3, when the theory is developed, it will be shown that the intensity of the scattering is related to the power of the laser used to excite the scattering, the square of the polarizability of the molecule analysed and the fourth power of the frequency chosen for the exciting laser. Thus, there is one molecular property, the polarizability, from which the molecular information will be derived and there are two instrumentation parameters which can be chosen by the spectroscopist. This choice is not straightforward. For example, since the scattering depends on the fourth power of the frequency, the obvious way of improving Raman sensitivity is to use the highest frequency possible, which would usually mean working in the UV region. UV excitation also has the advantage that there is less fluorescence than with visible excitation. However, many compounds absorb UV radiation. This and the high energy of the photons in this region means that there is a high risk of sample degradation through burning. It also means that the spectra may be rather different from normal Raman spectra due to resonance with any electronic transition which may cause absorption. This changes the relative intensities of the bands (see Chapter 4 for an explanation of resonance). Additionally, the lasers used can be quite expensive, there is a particular problem with safety since the beam is invisible and the quality of the optics required in the UV is very high. However, the rapid development of optical devices including laser diodes which work in the blue or UV, the unique information that can be obtained in this region and the improved sampling methods now available suggest that UV Raman scattering will be used more widely in the future. Further detail on the employment of UV Raman spectroscopy is given in Chapter 7.

Currently, most laboratories choose either a dispersive or an FT spectrometer. The former employs a visible laser for excitation, a dispersive spectrometer and a CCD for detection. The latter employs an NIR laser for excitation and an interferometer-based system which requires an FT program to produce the spectrum. Both types of instrument have their advantages and disadvantages. The choice for a particular laboratory very largely depends on the type of analysis to be carried out and the materials which the instrument is expected to examine.

## 2.3 VISIBLE EXCITATION

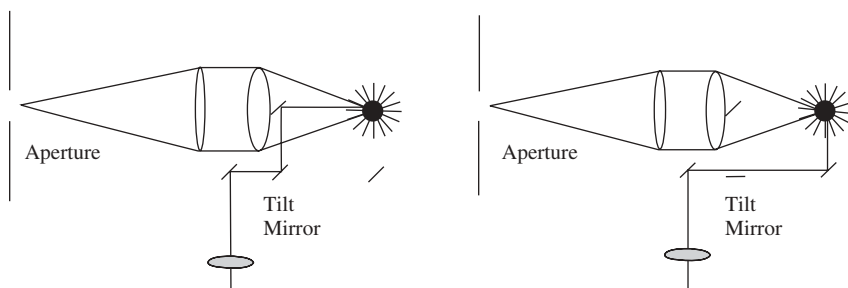
The most common choice is a visible laser for excitation. These laws are readily available and can be quite compact. Since peaks due to Raman scattering are sharper than the peaks usually detected in the visible region by absorbance and emission, and are measured as a shift from the energy of the excitation source,

a monochromatic source is required if quality data is to be obtained. As a result, good quality lasers have to be employed. However, in a modern instrument, weak and broad but recognizable spectra can be obtained even with low-powered, low-cost lasers. Raman scattering using a Raman microscope with a laser pointer has been recorded by the authors.

There are two basic geometries used in collecting Raman scattering:  $90^\circ$  scattering and  $180^\circ$  scattering (Figure 2.1). Both are effective. In  $90^\circ$  scattering, the laser beam is passed through the sample, say in a 1 cm cuvette, and the scattered light is collected at  $90^\circ$  by placing a lens in a suitable position. This light is then imaged onto the entrance slit of the Raman spectrometer. Since the light is scattered as a sphere, the larger the cone of light which can be collected the better. Consequently quite large lenses, or lenses with short focal lengths, are used to cover the largest practicable angle. It has to be remembered that this is not the only consideration. It is also necessary to use the monochromator efficiently and to image the collected light efficiently onto the detector. As a result, the collection lenses have to be matched to the collection optics for efficient performance.

In the  $180^\circ$  system, the laser is delivered through the collection lens and the scattered light collected back through it. In the arrangement shown below, a small mirror is placed in front of the collection lens to achieve this. This is the common arrangement in systems which use a microscope to collect the light. Sometimes a mirror system such as a Cassegranian system or a silvered sphere are used but lenses are more common. ‘Grazing incidence’ in which the laser beam is directed along the surface is sometimes used in special circumstances.

Some years ago, the spectrometers were quite large. To collect Raman scattering effectively it is necessary to remove the much more intense Rayleigh scattering and other light such as specular reflection from the surface of the sample. This light is much more intense than standard Raman scattering and can flood the detector especially if it is intended to detect Raman scattering which is close in energy to the laser frequency (i.e. low energy vibrations).

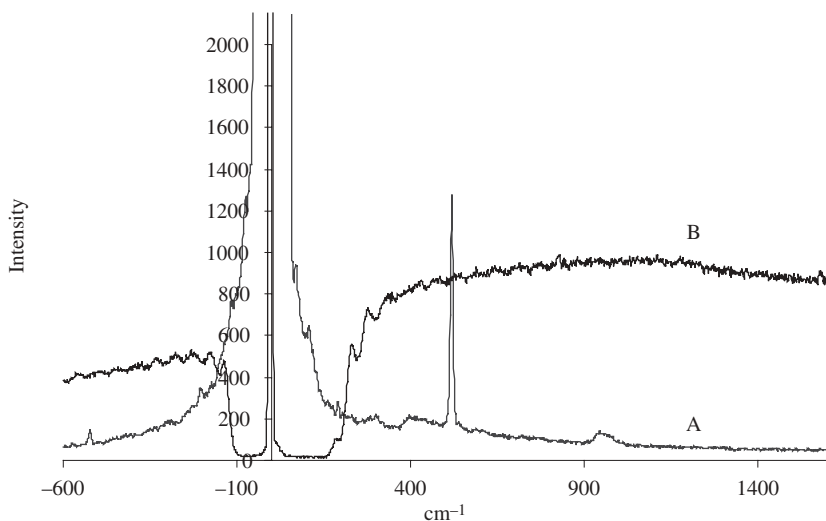


**Figure 2.1.**  $180^\circ$  (left) and  $90^\circ$  (right) scattering arrangements. The low beam is shown as arriving vertically through a lens and a set of mirrors onto the sample (the black dot) a cone of scattered light is then collected into the spectrometer.



Consequently some device has to be employed to separate the wavelength-shifted Raman scattering from the other light collected. This can be done with two or even three monochromators. The purpose of the first monochromator is mainly to separate the frequency-shifted Raman scattering from the other radiation. The second monochromator increases the dispersion and separates the individual Raman peaks. However, filter technology has improved with the development of effective notch and edge filters. The notch filter, in particular, is widely used. It is designed to absorb all light of the frequency of the incident laser light. Usually a filter which collects most of the light within  $200\text{ cm}^{-1}$  of the excitation frequency is regarded as sufficient (Figure 2.2). The range of frequencies absorbed depends on the quality of the filter and hence the choice is a cost/performance decision the instrument designer has to make. This filter in many instruments can be changed later though other optical re-alignments may also be necessary. Some experiments do require measurements closer to the exciting line. In these cases, the use of monochromators would still be the preferred method for separating the Raman scattering from other light.

The notch filter has a huge advantage in that it is small and efficient. This has very much reduced the size of Raman spectrometers and improved their efficiency. The notch filter type of spectrometer largely dominates the market. In the most



**Figure 2.2.** Raman spectra taken across the exciting line. In A the Raman band at  $520\text{ cm}^{-1}$  is much weaker than the signal from the non frequency shifted light. The second spectrum B is from a poor Raman scatterer with a notch filter in place. Close to the exciting line most scattering is removed by the filter with some laser breakthrough at the laser energy. The features on the edge of the region covered by the notch are artifacts caused by it and not Raman peaks.

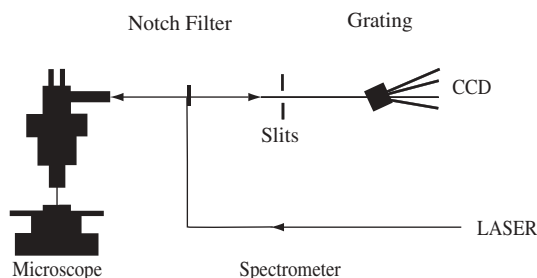
common type of instrument, the scattered light is collected through the notch filter and focussed into a monochromator which separates out the different energies of the Raman scattering. The radiation is then focussed onto a CCD. This is a sectorised piece of silicon in which each sector is separately addressed to the computer. In this way, it is possible to discriminate each frequency of the scattered light and therefore construct a spectrum of the type shown in Chapter 1. A CCD detector, in absolute terms of sensitivity per photon scattered, is not the most efficient detector in the visible region. However, the fact that all scattering is continually accumulated during the whole exposure of the sample to the exciting radiation more than compensates for this. The choice of a dispersive visible instrument is a good one if flexible sampling, ease of change of excitation wavelength or the use of techniques such as resonance Raman scattering (RR) is a priority.

There are three main disadvantages of this type of equipment. The older systems which used monochromators instead of a notch filter could be tuned to a range of excitation frequencies. To change the excitation frequency with a notch filter system requires that the filter be replaced with a filter of exactly the right frequency for the laser line chosen. Further, filter-based systems do not enable the recording of Raman scattering as close to the exciting line as is possible with the monochromator-based systems scattering at about  $10\text{ cm}^{-1}$  from the exciting line has been recorded using additional special filters. The development of simple, reliable, tuneable laser systems may mean that for some specialist Raman spectroscopists, the choice of a double or triple monochromator system may be the more realistic option. However, the simplicity and high state of development of notch filter systems means that these are likely to be the preferred choice for most spectroscopists.

The main disadvantage of using visible excitation is one which is common to all visible spectrometer systems and is a particularly serious one – fluorescence. This is a much bigger problem in the visible region than in either the UV or the NIR. Since Raman scattering is a weak effect, a powerful excitation source is chosen to provide a high power density at the sample. This means that not only can fluorescence occur from the sample being studied but also any minor contaminant which is fluorescent can give large signals. Since fluorescence will occur at energies below that of the excitation, it can be quite intense in the energy region covered by Stokes Raman scattering. Consequently it very often interferes and is probably the main reason visible Raman scattering is not more widely used.

### **2.3.1 Raman Microscopes**

On many modern Raman spectrometers, the sample is simply presented to a microscope which is an integral part of the spectrometer. The microscope has many advantages; for example, it is possible to look at extremely small samples and therefore, despite the fact that Raman scattering is weak, to detect very small amounts of material. Further, it can discriminate against fluorescence from a



**Figure 2.3.** Raman spectrometer and microscope, using a visible laser, notch filter, spectrometer and CCD detector.

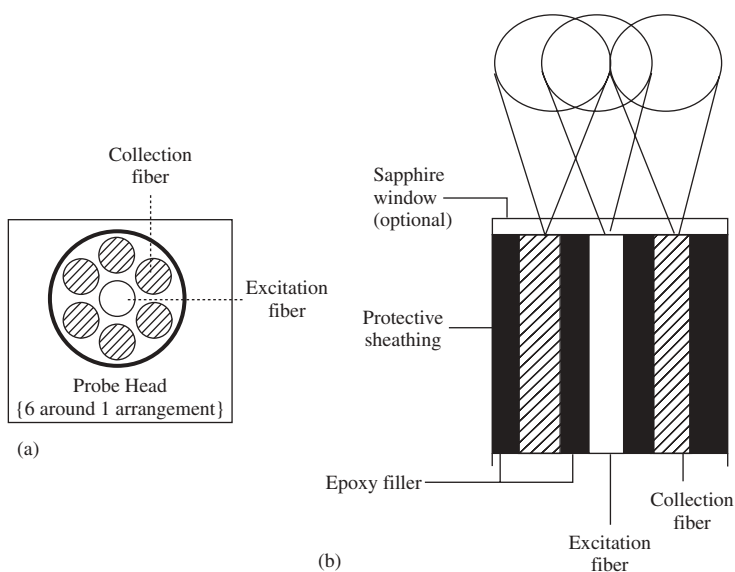
sample matrix since only the chosen microscopic feature in the sample is irradiated at high power, particularly when the microscope is set up confocally. The effects of this method of sample presentation are described more fully in Section 2.7.

This inherently simple technology has big advantages. Visible laser sources and optics are very good. The coupling of visible spectrometers to a microscope to separate the light collection at the sensing point from the detection system is extremely efficient. Figure 2.3 shows a typical arrangement for a microscope. In this arrangement, the laser is focussed through a pinhole and then collected as an expanded parallel beam. The reason for doing this is to fill the optics of the microscope. There is a plasma filter to remove any specious radiation such as weak emission from lines other than the main exciting line in the laser and any background radiation from the laser. The radiation is then arranged to hit a notch filter. These are interference filters, which work well when the beam is perpendicular to the plane of the filter. At the angle shown in the diagram, the laser radiation contacts the filter so that the light is entirely reflected into the microscope. Once the scattered radiation is collected from the microscope back through the same optics, the beam is incident on the filter at the ideal angle for transmission of the scattered radiation. This light is then passed into the monochromator as shown and onto the CCD detector. Raman spectrometers also have polarizing optics before and after the sample, which is dealt with in Chapter 3.

Another common choice of collection system, owing to the flexibility of fibre optics, is a small probe, designed to excite the sample, coupled to a remote monochromator and detector to collect the scattering. This system is very flexible. There are many uses for which this may be preferred; these are discussed in Section 2.6.5.

### 2.3.2 Fibre Optic Coupling and Wave Guides

In many applications the use of fibre optics to separate the sampling head from the spectrometer can be a big advantage (Figure 2.4). For example Raman



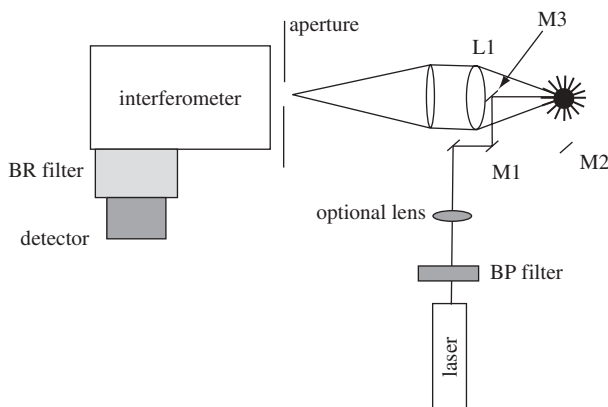
**Figure 2.4.** Fiber optic probe end. (Reproduced from J.B. Slater, J.M. Tedesco, R.C. Fairchild and I.R. Lewis, 'Raman spectrometry and its adaptation to the industrial environment' in: *Handbook of Raman Spectroscopy*, Ch. 3, I.R. Lewis and H.G.M. Edwards (eds), Marcel Dekker, New York, 2001, pp. 41–144.)

spectroscopy can be used for on-line analysis on a chemical plant where access can be difficult and the environment not suitable for spectroscopy perhaps because the plant is open to the elements, there is dust from delivery lorries or there simply is no space. However, with fibre optics, only the bead used can be exposed with the expensive spectrometer housed elsewhere. Further, with portable equipment now becoming common and although not necessary for all portable devices, it can be convenient to have a spectrometer which can be held in one hand and a simple small probe in the other. It is also possible to armour these probes to prevent damage. Thus, the use of fibre optics has extended the utility of Raman spectroscopy considerably. One problem that arises is that while passing down the fibre optic, the laser light excites Raman scattering from the fibre optic material itself. This can act as an interference, particularly if the scattering from the sample is weak and a large length of fibre optic cable is used. The main problem comes from Raman scattering produced by the laser beam which can travel in both directions in the fibre. One way of overcoming the problem is to use a multi-mode cable in which the laser is launched down some fibres on the outside and collected through a single central fibre. Usually, the notch filter is placed as close to the collection point as is possible since this will cut out any reflected light or Rayleigh scattering before the Raman scattered light is collected down the fibre. With this arrangement, fibre optic

coupling of a sampling head to a Raman spectrometer is an extremely effective way of collecting Raman scattering with big advantages in flexibility.

## 2.4 NIR EXCITATION

In some laboratories, the overriding criterion for the purchase of a Raman system is that as many samples as possible will give a Raman spectrum. This will be true, for example, in an industrial laboratory where the nature of the next batch of samples cannot be known or controlled. In this case, the use of a NIR laser and an interferometer with detection using an FT program may well be the correct choice (Figure 2.5). The main advantage of the system is that it uses a NIR laser, usually a neodymium-doped yttrium aluminium garnet ( $\text{Nd}^{3+}$ :YAG) solid state laser emitting at 1064 nm. As a result, few molecules have excited states low enough in energy to give fluorescence. This largely, but not completely, gets round the problem of fluorescence. However, the Raman scattering is inherently weaker because the energy of the radiation is lower and the fourth power law applies. However, since the exciting radiation does not absorb into most samples as efficiently as visible radiation, the laser powers useable are relatively high (up to 2 watts). Further the interferometer detection system, which is essentially the FT-based system used in infrared spectrometers, is very sensitive. The detectors normally used at room temperature are InGaAs detectors which can be cooled to liquid nitrogen temperatures for a slight increase in sensitivity. This type of instrument can also be coupled to a microscope but



**Figure 2.5.** NIR FT instrument schematic. The arrangement for collecting the light is very similar to that for a dispersive spectrometer (see Figure 2.1). (Reproduced from Richard L. McCreery, *Raman Spectroscopy for Chemical Analysis*, John Wiley & Sons, Inc., New York, 2000.)

the high power density at the focal point gives an increased tendency to thermal degradation. Very occasionally a sample will fluoresce, but for most samples this is not a problem. Thus, this instrument is closer to an infrared system in that it can record Raman scattering from a wide range of materials present in different states. Compared with infrared absorption spectrometers, the system has its own unique advantages. It is non-contact and samples require little or no preparation. For example, the stringency of the optical system is reduced compared to that of visible systems. Thus, although it is often quite simple to use a visible system to look at a sample in a bottle, this is easier in the NIR because dispersion from non-ideal surfaces is less important and there is less chance of fluorescence from containers.

A comparison of the visible and NIR/FT instruments is made more complex by the fact that the wavelength range of the visible instruments has been extended by using NIR lasers with excitation lines in the 790–850 nm wavelength region. The major problem for the manufacturers of visible source instruments is that the CCD chips lack sensitivity at wavelengths above 1000 nm. This means that lasers that operate at 790 nm or 850 nm are effective but are also very close to the end of the detector range. This can lead to a drop in sensitivity for higher frequency peaks. However these systems increase the range of samples for which Raman scattering can be measured effectively using visible excitation without fluorescence interference.

The range of choice of Raman spectrometers is ever increasing and the size and cost are dropping. A fascinating new development is the production of monochromators with relatively simple CCD detectors which are approximately  $4'' \times 2'' \times 2''$  and which use fibre optic coupled sensing. This makes truly portable Raman spectroscopy a much more practical proposition especially since these instruments tend to use simpler CCD detectors which are of lower price than the lab-based instruments.

## **2.5 RAMAN SAMPLE PREPARATION AND HANDLING**

Raman spectroscopy, as a scattering technique, is well known for the minimum of sample handling and preparation that is required. Hendra's rubber duck [1] is a typical example. A small, children's duck thought to be made of rubber was placed directly in the spectrometer beam. Almost immediately a Raman spectrum was recorded of polypropylene! Whilst a large range of homogeneous materials can be examined this way, many samples require some form of preparation and/or mounting in a spectrometer. Compared with infrared spectroscopy, fewer accessories are commercially available though many can be used for both techniques. Typical Raman accessories are powder sample holders, cuvette holders, small liquid sample holders (cf. NMR sample tubes) and clamps for irregularly shaped objects. In the past few years there has also

been an increase in the development of specialist cells for rotating solids, vapour cells, reaction cells and variable temperature or pressure cells. In the following section several ways of handling and mounting samples are described, with some advantages, disadvantages and precautions. A review article by Bowie *et al.* [2] has highlighted some of the effects on FT Raman spectra which can originate from the sample. This section gives some examples of how to overcome the more common effects.

Many organic, and inorganic, materials are suitable for Raman spectroscopic analysis. These can be solids, liquids, polymers or vapours. The majority of bulk, industrial laboratory samples are powders or liquids and can be examined directly by Raman spectroscopy at room temperature. Accessories for examination of materials by Raman spectroscopy are available across a wide range of temperature and physical forms. Sample presentation is rarely an issue in Raman spectroscopy of bulk samples. Many materials can be mounted directly in the beam as neat powders, polymer films, etc. The authors have examined liquids and powders presented in glass containers from capillary tubes, through vials, to 500 ml brown bottles. Samples have also been examined in polymer containers. Raman spectroscopy is less demanding of beam position, for qualitative work with bulk samples, as the radiation is scattered. However, the sample can be optimized in the beam, particularly necessary for quantitative studies, but the collection solid angle has to be considered. On some occasions the angle of the sample to the scattered beam, i.e.  $90^\circ$  or  $180^\circ$ , will lead to orientation effects. Crystalline samples should be considered from this point of view. Rotating the sample in the beam can average out these effects. Particle size effects have also been reported. The largest problems with samples for Raman spectroscopy occur from fluorescence or burning. Fluorescence arising from an impurity can, in some cases, be burnt out by leaving the sample in the beam for a few minutes or overnight. This works because there is specific absorption of the light into the fluorophore so that it is preferentially degraded. However, particularly with coloured samples, absorption by the sample can cause degradation of the sample itself. Again this can be reduced by rotating the sample. The speed of rotation has to be kept  $<50$  Hz in FT Raman spectrometers or beats will be seen across the spectrum. An alternative way to reduce the burning effects is to disperse the sample in other media without a Raman spectrum such as KBr or KCl.

With this type of analysis, one must consider the differing Raman scattering intensities of the analyte and the surrounding matrix and also the possibility of contamination. This is particularly important in Raman scattering since spectral intensities can vary quite widely from one substance to another and if the impurity has a strong spectra (or is resonant, Chapter 4) then that spectra can dominate or be an appreciable factor in the final spectrum. There are a number of examples in the literature where this simple precaution has been ignored and important conclusions drawn from data which subsequently has been shown to

have arisen from a contaminant. With samples that are in a matrix, e.g. a container or a solution, the relative scattering intensities of the container and the sample need to be considered before the spectra are recorded or interpretation is attempted. An empty polythene bottle placed in the beam will show bands due to polythene. Fill the bottle with sulphur and only the sulphur bands will be observed as the polythene is a much weaker Raman scatterer. Water is a strong absorber of infrared radiation, as is glass. Both are weak scatterers in Raman spectroscopy, which makes the technique particularly suitable for samples in aqueous solutions and/or in glass containers. Glass and water do have their own spectra but only need to be considered with weak solutions.

Small samples may have to be examined with a microscope or microprobe but this means that the beam diameter reduces very significantly and is often much smaller than the total size of the sample. The focal point will then determine which part of the sample is being analysed. This means that it is important to check the homogeneity of the sample by taking a number of measurements across it. It becomes particularly important when larger samples are used with the microscope simply for convenience. The relative refractive indices of the sample and matrix may also have an effect. This is particularly important when attempting confocal Raman microscopy and will be dealt with in Section 2.7.

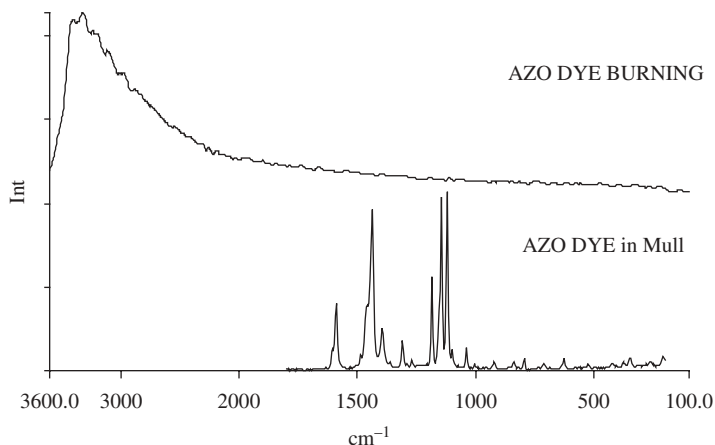
### **2.5.1 Raman Sample Handling**

Many powders and liquids can be examined by placing the container in which they are supplied directly in the beam. For example, if the sample is supplied in a bottle or vial and the sample gives a strong spectrum, the shape and colour of the vial or bottle is of little importance. Samples have been examined successfully, by the authors, in brown and plastic bottles as well as clear vials. The only constraints are that the outside of the container be clean, free from fingerprints, which cause fluorescence, and the labels do not obscure the sample. If the samples are weak Raman scatterers, then the spectra of the containers can interfere with the spectra of the samples. Not all samples can be examined directly, due to a weak signal, burning or fluorescence. A number of techniques have been developed which reduce some effects and enhance the spectra. Further, plastic cuvettes and microtiter plates can be used with both visible and FT systems. It is important that the laser is focussed into the sample and away from the walls of the cuvette or the sides and foot of the microtiter plate. When this is done, the significantly higher power density of the sample mitigates any interference from the cuvettes or microtiter plates. However, if the sample is focussed onto these materials, excellent spectra can often be obtained from the polymer. Thus, although such systems can conveniently be used and for reasons of cost where repeated measurements are required they may well be the preferred technique, it is essential that the Raman spectroscopist is aware of the possible dangers of the method.



Neat powders with weak signals can be mounted in loosely filled containers or in a compacted solids holder. The authors used the latter technique successfully with a crystalline, low density fungicide which was moved away from the bottle wall by the laser beam power, but gave a strong spectrum 'fixed' in the holder. However, with samples that are crystalline, orientation effects can change the spectra as can the particle size of powders. Using inorganic material it has been shown that the Raman intensity increases as the particle size decreases [3–5]. The theoretical dependence has been described by Schrader and Bergmann [6]. Experimental work has shown that a general fit can be obtained. However, if a sample is dispersed in a matrix, e.g. filler in a polymer or paint resin, droplets in an emulsion, then a sudden in rapid reduction Raman signal can occur at particular sizes below the wavelength of illumination. An example of this is titanium dioxide which gives characteristic Raman spectra in the bulk solid state but gives weak or no spectra when dispersed as a filler in polythene.

Samples of neat powders which are too small to fill the beam or which burn in a bottle can be prepared as a halide disk in a similar way for infrared examination. Strong spectra have been recorded at high laser powers (1400 mw), without burning, by this method. With samples that strongly absorb and burn, very early conventional dispersive Raman instruments employed a sample-spinning device to constantly refresh the sample in the beam. These can cause 'beats' in an FT spectrum, unless the rotation is very slow (<50 Hz). Accessories are now available which will turn samples at this speed [7]. Very sensitive or strongly absorbing samples can burn at very low levels of laser power. The preparation of samples in the same way as hydrocarbon oil mulls (Figure 2.6) for infrared, between salt



**Figure 2.6.** Neat sample burning vs. mull spectrum. (Reproduced from J.M. Chalmers and G. Dent, in: *Industrial Analysis with Vibrational Spectroscopy*, Royal Society of Chemistry, London, 1997.)

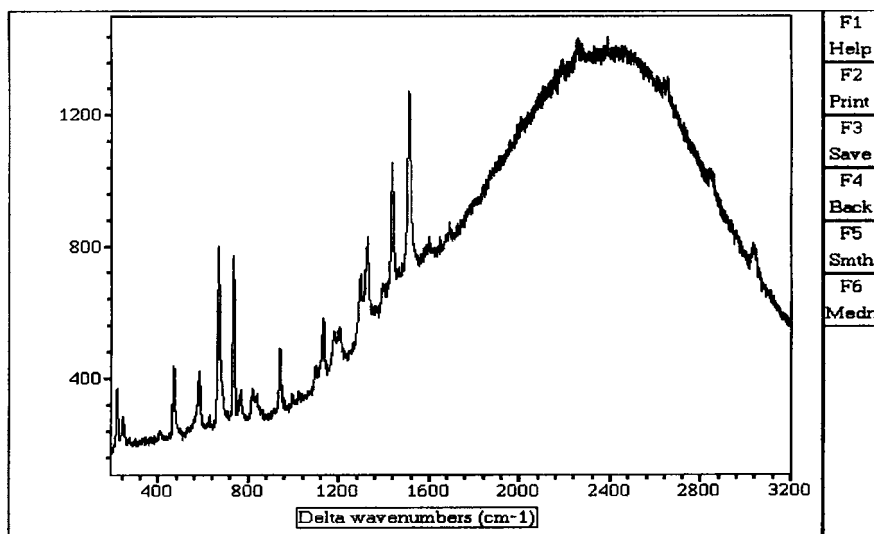
flats, give good, strong spectra [8]. Even some black samples can be examined by NIR FT Raman at laser powers of 1400 mw. This preparation technique also preserves physical form for polymorphism studies.

A study of the various diluents concluded that KCl was often the best diluent [9]. The process of forming the disks requires pressure and can cause changes in the sample; consequently the making of disks has to be avoided if changes such as polymorphism are suspected or are required to be studied. As already stated, spinning the sample, whilst successful with visible laser sources, has to be kept below 60 Hz with NIR FT Raman spectrometers. The other major difficulty encountered in visible spectrometers is fluorescence. The Raman effect is relatively weak with only  $\sim 1$  in  $10^4$  photons interacting with a molecule exhibiting the effect. Fluorescence is generated by very similar interactions with the molecule but is much stronger. Raman spectra can be totally dominated by the broadband fluorescence. Visible laser spectrometers can be used to attempt to burn out the fluorescence by leaving the sample under the beam for some time before measuring the scattering. This may take a few seconds or several hours, or may not occur at all. Moving to higher wavelengths of excitation can significantly reduce fluorescence. Visible lasers with an emitting wavelength of 765 nm have been developed with this advantage in mind. Fluorescence is very much reduced by operating FT Raman spectrometers, with laser sources in the near-infrared at 1064 nm. Although fluorescence is much reduced at 1064 nm, there are cases where even at this wavelength excitation can cause this problem.

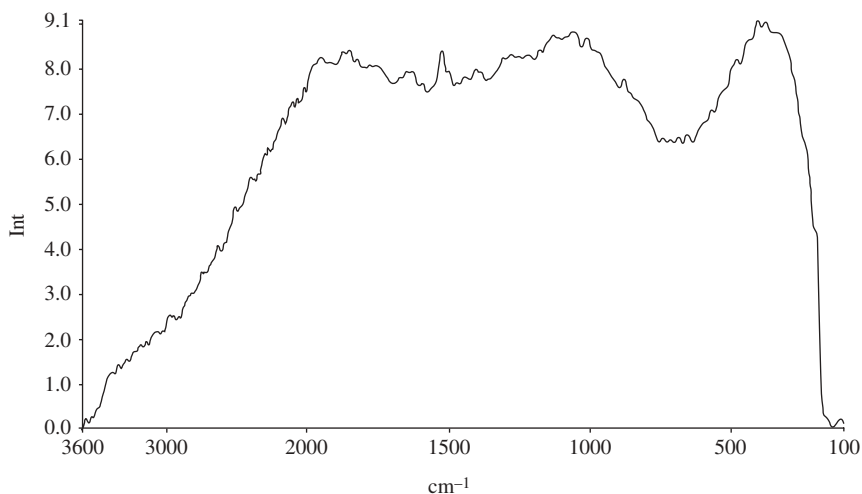
Copper phthalocyanine, discussed previously, is unusual in that the visible Raman spectrum shows some background fluorescence (Figure 2.7); the fluorescence increases with exciting frequencies towards the infrared. Early work by the authors showed that blue, green, red, yellow, some brown and even black samples could be examined by FT Raman spectroscopy, but blues and greens based on CuPc would still fluoresce. However, this gives a very characteristic Raman spectrum of many copper phthalocyanine-based materials which show broad fluorescence across the spectrum at 1064 nm excitation.

On increasing the exciting wavelength to 1339 nm, the fluorescence is much reduced and bands due to copper phthalocyanine spectrum reappear. It has been suggested [10] that this strange phenomenon is due to transition metals being present in the phthalocyanine ring. However, this is limited mainly to copper as shown by the spectra, recorded with 1064 nm excitation, of various other metal-substituted phthalocyanines, including metal-free phthalocyanine [11], shown in Figures 2.8 and 2.9. The spectrum of CuPc shown in this figure was obtained by making a very dilute disk (1:1000) in powdered silver reducing fluorescence.

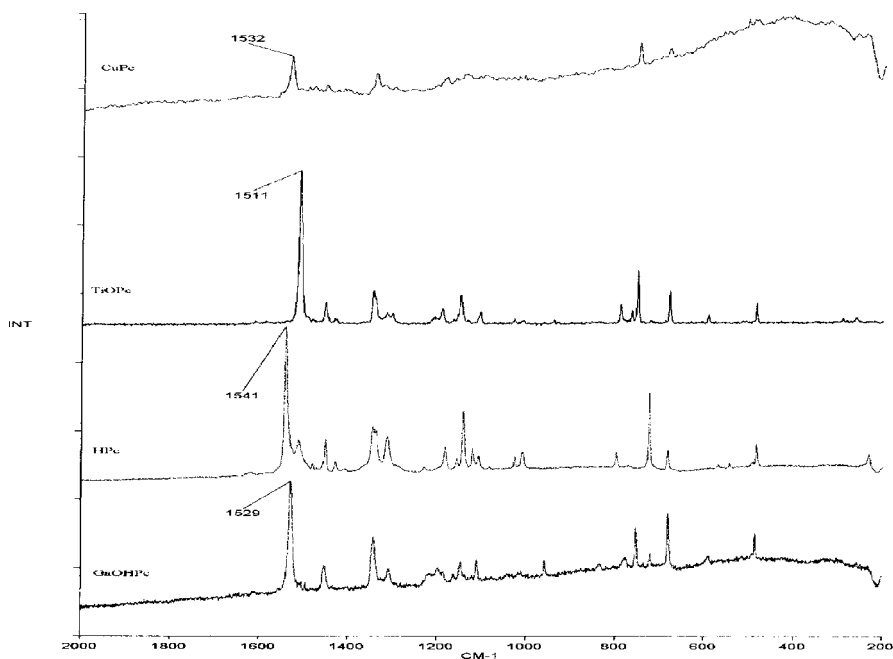
Colour is no guide as to whether a sample will fluoresce. Clear, water white crystals have been observed to cause fluorescence at all illuminating wavelengths. The sensitivity of the Raman spectrum is directly proportional to the exciting wavelength. Spectra obtained at 1064 nm excitation will be less



**Figure 2.7.** Raman spectrum of copper phthalocyanine with 632 nm excitation. (Reproduced from J. Chalmers and P. Griffiths (eds), *Handbook of Vibrational Spectroscopy*, vol. 4, John Wiley & Sons, Inc., New York, 2001, pp. 2593–2600.)



**Figure 2.8.** Raman spectrum of copper phthalocyanine with 1064 nm excitation. (Reproduced from NIR FT Raman examination phthalocyanines at 1064 nm, G. Dent and F. Farrell, *Spectrochim. Acta*, 1997, 53A, 1, 21 © 1997 by kind permission of Elsevier Science-NL, Sara Burgerhartstraat 25, 1055 KV Amsterdam, The Netherlands.)



**Figure 2.9.** NIR FT Raman spectra of phthalocyanines with various metals. (Reproduced from NIR FT Raman examination phthalocyanines at 1064 nm, G. Dent and F. Farrell, *Spectrochim. Acta*, 1997, 53A, 1, 21 © 1997 by kind permission of Elsevier Science-NL, Sara Burgerhartstraat 25, 1055 KV Amsterdam, The Netherlands.)

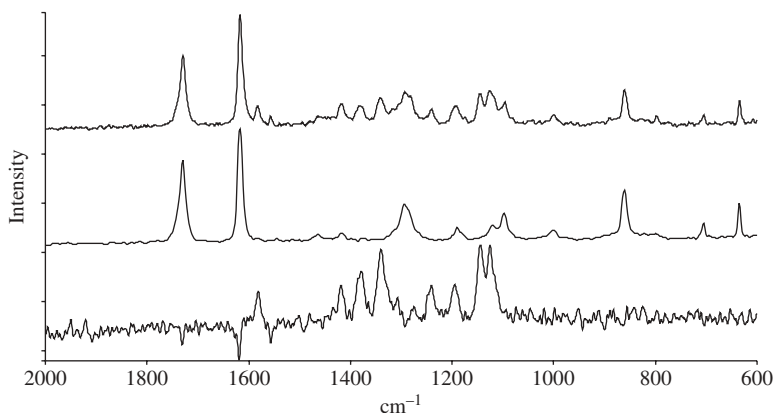
sensitive than spectra recorded at 765 nm. The fast multiscanning of FT spectrometers helps to mitigate but does not overcome this difference. By moving to lower wavelengths and into the UV, fluorescence is again much reduced. The sensitivity increases but the likelihood of thermal degradation also increases. Even at these wavelengths some solid samples still exhibit fluorescence. Liquids can suffer from fluorescence, but rarely suffer from burning. This is due to their high mobility and hence high heat capacity. If the samples are relatively clear or lightly coloured, spectra can be enhanced by placing the samples in silvered holders. These reflect the signals back through the sample onto the detector. Only small samples can be examined this way or the radiation will be self-absorbed. This effect was demonstrated with tetrahydrofuran (THF) where the  $917\text{ cm}^{-1}$  band when excited using 1064 nm has an absolute position of  $\sim 8478\text{ cm}^{-1}$ . This is almost at the peak of the NIR absorption band due to the second overtone of the  $-\text{C}-\text{H}$  stretch. Hence, as the path length is varied, the strength of the band will be attenuated due to the self-absorption [12, 13]. Self-absorption has also been observed when using visible lasers in resonance studies.

Polymers of all shapes and sizes can be examined by Raman spectroscopy. Safety spectacles, rolls, thin films, bottles and moulded platens have been examined by this technique. There is a lot of published literature on the Raman spectra of polymers for identification, structural behaviour and morphological properties (see Section 7.3). Polymers are, in general, relatively weak scatterers. This can either be regarded a problem or be used to advantage. As mentioned earlier, samples can be examined in plastic bottles. Sulphur gives a very strong Raman spectrum with no evidence of the bottle wall in the spectrum. On the other hand, the spectrum of a 2% azo dye in polymer film shows both bands due to both dye and polymer.

In examining a polymer film one recommendation is to fold the film as many times as possible to create a 'thick' layer. In this case any orientation effects will be lost. Sometimes film samples are not big enough to fold. An enhanced, strong spectrum can be recorded by placing a small, single sheet flat across the mirrored back face holder. Spectra of coloured polyethylene terephthalate have been recorded this way with strong enough bands to see both the dye and the film. In Figure 2.10 the spectra of both clear film and dyed film were recorded by this technique. The resulting spectrum from a spectral subtraction clearly shows the bands due to the dye.

### 2.5.2 Sample Mounting – Optical Considerations

As can be seen from the foregoing descriptions, sample preparation and mounting can be relatively simple and flexible. However, if reproducible spectra or quantitation is required, then the optics of the beam and sample presentation needs to be considered. As already described, most spectrometers



**Figure 2.10.** Raman spectra of dye in fibre. The top spectrum is from the dyed fibre, the middle one is from the fibre and the foot one is the difference.

collect at a nominal angle of either  $90^\circ$  or  $180^\circ$  to the exciting laser beam. It is the latter aspect which makes the technique so versatile. Also, the radiation is not emitted from a point source. One of the factors which determines the strength of the spectrum is the number of molecules in the sampling volume created by the focussed beam. The sampling volume is the volume of sample irradiated with high power density. It can be a complex state (see Figure 2.11). It can be considered as a cylinder calculated by choosing a power density below which appreciable Raman scattering is not expected (Figure 2.11). The depth of this cylinder is then the distance between the converging beam above the sample with that power density and the diverging beam below the sample with the same power density. The diameter is the diameter of the beam at those points. Clearly, there is no such cut-off point and some scattering may be expected from above and below these lines. The amount will be determined by whether or not the Raman microscope has been set up to be confocal. It is not normally regarded as worthwhile to model the more complex geometric shapes obtained in practice. One good reason for this is that refraction between different fluids and gases causes dispersion of the beam and this is not taken into account in this calculation.

$$D = 4\lambda f / \pi d,$$

$$L = 16\lambda f^2 / \pi d^2,$$

$D$  = diameter of cylinder,

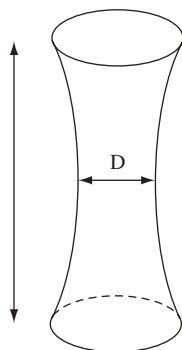
$L$  = length of cylinder,

$\lambda$  = laser wavelength,

$d$  = diameter of unfocussed laser beam,

$f$  = focal length of focussing lens.

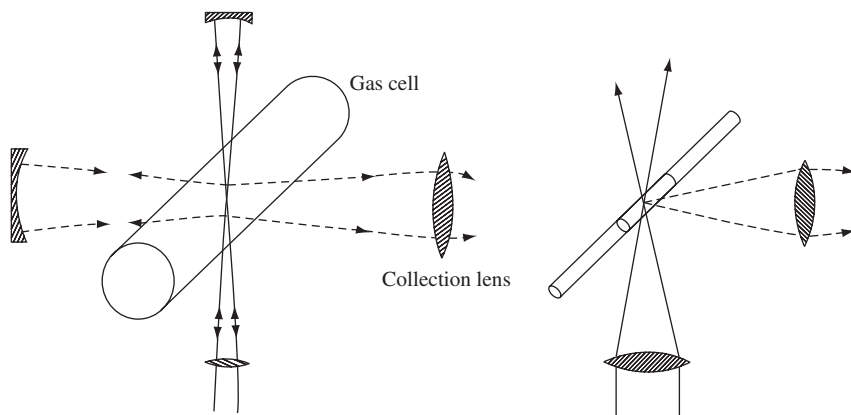
This volume can be used to estimate approximately the number of molecules being interrogated in the system at any one time. In the case of a gas, the



**Figure 2.11.** Sampling volume for a simple case.

number of molecules will be quite low. As a result, for gas phase measurements, instead of focussing the beam tightly, very long cells are often used. Sensitivity can be increased by using concave mirrors to reflect the exciting and scattered beams back through the sample (Figure 2.12) and in some gas cells, a multiple pass system reflects the beam many times to increase sensitivity. Similar arrangements can be made for liquids but these are usually less necessary due to the higher concentration of molecules in the same volume.

For solids and liquids, as stated earlier, collection should be from as large a cone of scattering as possible. Sensitivity can be improved by using a reflective surface behind the sample tube/vessel. In the case of a modified FT spectrometer, radiation is passed through the Jacquinot stop, which can have a diameter of a few millimetres, or in the case of the visible spectrometer, it is focussed onto the entry slits of the monochromator. To obtain the maximum signal from a homogeneous solid, the surface of the solid should be at, or close to, the focal point. In many cases, acceptable spectra can be obtained from samples not at the focal point. It has been shown that relative band strengths can vary depending on the distance the sample is mounted from this point. Whilst this is not always significant in identification, quantification could be seriously affected [14]. For liquids and gases, the system can be improved further by creating a completely reflecting sphere which gives multiple reflection inside the surface and allows only egress from the sphere through a cone which is collected directly by a lens or is directly focussed into the spectrometer.



**Figure 2.12.** Gas cell and capillary tube both with 90° collection angle. The gas cell shows a double pass system to improve sensitivity. (D. Loudon, in: *Laboratory Methods in Vibrational Spectroscopy*, H.A. Willis, J.H. van der Mass and R.J. Miller (eds), John Wiley & Sons, Inc., New York, 1987.)

## **2.6 SAMPLE MOUNTING ACCESSORIES**

### **2.6.1 Small Fibres, Films, Liquids and Powders**

Many samples that cannot be examined directly can easily be mounted at the optimum point by the use of small-diameter glass tubes. NMR sample tubes are often used for liquids, or loosely packed solids, and are easily held in position. Solids can also be held in the open end of the tube, then mounted so that the beam is focussed onto the powder rather than through the glass wall. If the powder in the main part of the tube exhibits thermal degradation (burning), then slowly rotating the tube constantly refreshes the exposed surface. Fibres and thin polymer films can be examined by loosely packing into the tubes or by wrapping round the outside of the tube until a thickness is achieved which will provide a spectrum with a required S/N ratio. Again if burning occurs, the tube can be slowly rotated. Polymers and fibres can also be examined by wrapping them around a glass microscope slide but this would be difficult to rotate. Special cells have been designed [15] to examine fibres and fabrics which involve both sample compression and a back-scattering mirror. The cell also contains a windowless aperture. Previously it was stated that powders which are strongly absorbing can be diluted by KCl, KBr, Nujol, etc. These samples can be mounted in glass tubes in the same way as the neat powders, or prepared as disks and mulls in the same way as they would be for infrared examination.

### **2.6.2 Variable Temperature and Pressure Cells**

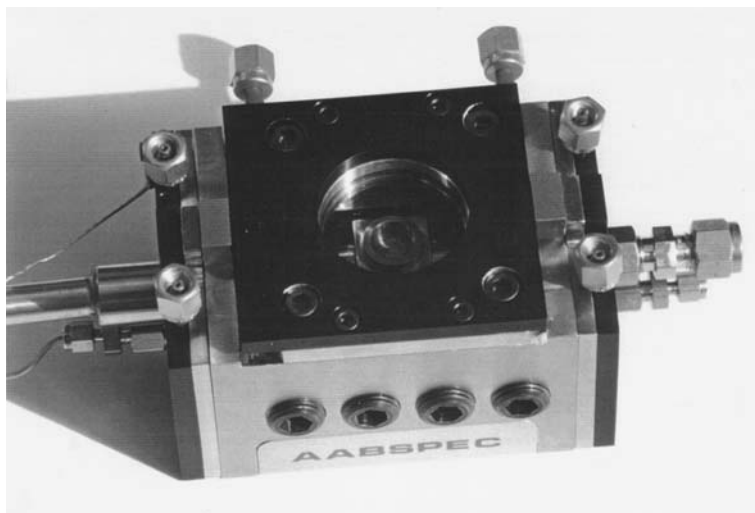
Whilst sample heating can be seen as a problem in some cases, there are often requirements to record spectra of samples over a temperature range, both above and below room temperature. This is an area where a wide range of specifically designed cells have been reported to fulfill the requirement for both dispersive and FT spectrometers (Figure 2.13). Cells have been designed to work across a temperature range of  $-170$ – $950^{\circ}\text{C}$  and from high vacuum to 10,000 psig. The difficulty often encountered is in making sealable windows of the optical material – quartz, sapphire and diamond have been used.

Diamond is particularly useful in anvil cells where pressures  $>1000$  atm can be encountered. Whilst samples can be examined over a range of temperatures for reaction rates, morphological changes and degradation studies through Raman spectroscopy can be used in reverse as a temperature probe. By measuring the relative intensities of pairs of bands in the Stokes and anti-Stokes spectra and applying the Maxwell–Boltzman equation (see Chapter 3) the temperature of a sample can be determined.

### **2.6.3 Special Applications – Thin Films and Catalysts**

The examples described so far have been of relatively large bulk samples, and microscopically small samples will be dealt with in Section 2.7. There are





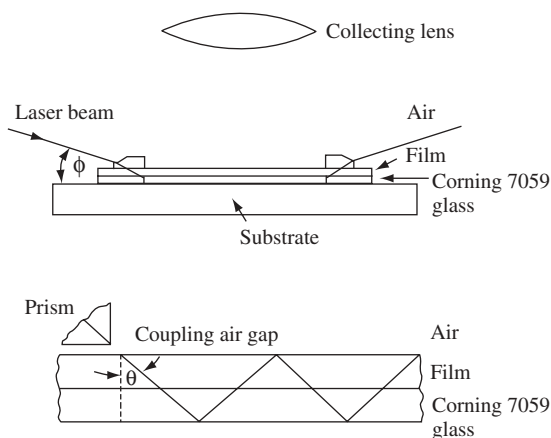
**Figure 2.13.** AABSPEC variable temperature and pressure cell. (With permission of AABSPEC.)

occasions when less common applications are required. One of these is the study of thin films. Various sampling techniques have been applied, during early modern development of Raman spectroscopy, to obtain spectra at micron or nanometre scales. These were reviewed by Loudon [16] for visible spectrometers and include interference enhancement, surface enhancement and attenuated total reflection/total internal reflection.

Figure 2.14 shows an arrangement for examining thin films at a glancing angle with internal reflections along the film enhancing the signal. The scattering nature of Raman spectroscopy at  $90^\circ$  or  $180^\circ$  particularly lends itself to surface studies. SER and SERRS enhancements are described in Chapter 5. However, samples held on solid support materials are open to study, with one of the most common being pyridine, which led to the discovery of the SERS effect [17]. This ability to examine surfaces and interfaces which has led to a number of specifically designed cells for catalysts on electrochemical surfaces at various temperatures and pressures. A typical reaction cell is shown in Figure 2.15.

#### **2.6.4 Flow Through/Reaction Cells and Sample Changers, Automated Mounts**

The cells and systems described in this chapter have been on static samples which in many spectroscopists' eyes are a pre-requisite for Raman spectroscopy. Reacting systems, flowing systems or systems which change samples are requirements for the modern spectroscopist. The advantages of Raman



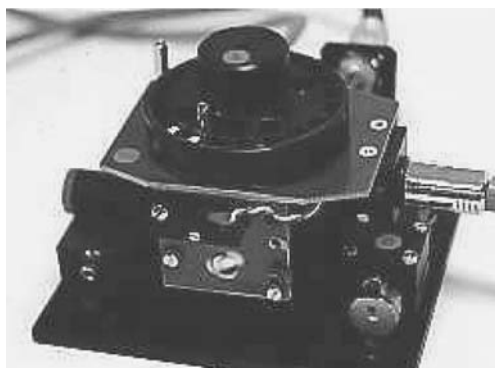
**Figure 2.14.** Arrangements for measuring thin films. (Reproduced with permission from J.F. Rabolt, R. Santo and J.D. Swalen, *Applied Spectroscopy*, **34**, 517 (1980).)



**Figure 2.15.** Renishaw cell. (SPD/PN/089 Issue 1.0 June 2003, Product note from the Spectroscopy Products Division.)

spectroscopy, previously described, both in scattering and in being able to probe through glass, provide a great flexibility in approach. Small cells can be simply developed with a glass window for reaction monitoring or simple glass tubes can be used for flow through systems. Automated sample changers have been developed for the semi-continuous examination of pharmaceutical tablets and a combined macro/micro sampling stage has also been developed (Figure 2.16).

In all cases, whilst path length is a minor consideration, the experiment and/or accessory has to be designed to ensure that the feature of interest matches the beam and the focal point for reproducibility and quantitative considerations



**Figure 2.16.** Pharmaceutical tablet autochanger. (With permission of Vентаcon Ltd.)

(see Section 2.9.3). Other common forms of sample handling are the microtiter plates used in biology. The advantage of these plates is that they allow for multiple analysis simple. Modern Raman spectrometers can give results in a few seconds and the sample can be moved under the beam using software and a sample positioning stage and this is used in mapping is described elsewhere in this book (Section 2.7). Capillaries also are excellent sample holders for Raman scattering. There is some distortion from the walls of some capillaries and this can cause a low background. However, it is possible to seal small samples, single crystals or air-sensitive material inside a capillary and transport it to the spectrometer. No further sample preparation is required. Quartz capillaries and square capillaries can reduce the background significantly.

### 2.6.5 Fibre Optic and Guided Wave Sensing

This chapter has been primarily concerned with mounting samples in the beam of the spectrometer mainly in the sample compartment. As explained in Section 2.3 the versatility of the technique can be extended by the use of fibre optic probes [18]. We have already described large glass containers being placed in the spectrometer beam. The reverse situation is to take the beam to, or as near as possible to, the sample. For example, the probe can be inserted into a chemical reactor or used to focus on a sample in a container where the environment is hostile or the geometry awkward. By using the transparency of glass, long fibres can be used to examine reactions in vessels from tens to hundreds of metres from the spectrometer on an industrial plant. Some applications are described in Section 6.9. The probes give a high background silicate signal for NIR radiation limiting the distance. Spectra of aspirin tablets have been reported at 50 m using band pass filters [19]. Materials which cannot be introduced into the spectrometer due to their physical size or hazardous nature

can have the beam brought to the sample surface. By fixing a lens on the end of the fibre optic probe to focus the beam and act as the  $180^\circ$  collecting window, samples can be examined *in situ*. If a fibre can be pointed at the sample, the spectrum can be measured. Samples which are smaller than the beam diameter can be examined on a microscope by selective use of apertures. The smallest samples examined in this way are theoretically  $\sim 1\mu\text{m}$  in diameter. This is referred to as the diffraction limit due to the wavelength of the irradiating beam. Applications have been reported [20] where the diffraction limit has apparently been defeated by coupling a fibre optic Raman probe with an atomic force microscope (AFM). In this method, the fibre is metal-coated which prevents egress of the beam from the fibre. It is then heated and drawn out so that an aperture is created at the fibre tip which is typically between 100 and 50 nm in diameter. The light as it passes through the fibre is compressed so that it emerges and rapidly expands from the small aperture. Thus if the tip is placed almost on a surface by the AFM head, the effective excitation area is very small and below the diffraction limit. This process can be reversed where the laser excites the surface externally and the fibre picks up the scattered light. The main problem with the method is that it is inefficient and requires good Raman scatterers to be effective. This is often referred to as scanning near-field optical microscopy (SNOM) which will be discussed in Chapter 7.

Another way of obtaining Raman scattering, which is becoming increasingly popular, is to use waveguiding. In this approach narrow tubes with high-refractive-index tube wall materials are filled with the analyte and the laser beam is launched down the tube so that it is contained in the analyte solution. The signal is then collected at the other end, passed through a notch filter and analysed in a standard Raman spectrometer. The advantage of this arrangement is that there is a very long path length and the laser irradiates the whole sample so that quite dilute solutions can be analysed. The prime requirement is that the sample has a higher refractive index than the sample tube to constrain the illuminating light within the tube and to achieve total internal reflection. This reduces the number of liquids or vapours which can be analysed. Spectra of benzene and weak solutions of sodium carbonate and  $\beta$ -carotene have been recorded [21, 22]. One alternative is to coat the inside of the cell with a high reflective coating such as gold. However this can be limiting in cost and optical sampling arrangements. Another option is to use silver to produce an SERS active surface. Detection limits of less than  $10^{-9}$  mol/L in low refractive index liquids have been reported [23] by using this technique.

## 2.7 MICROSCOPY

As already mentioned in this chapter Raman spectrometers can have microscopes as an inherent part of the instrument or be easily coupled. The ease of coupling

and ability to employ microscopes as sampling accessories comes from the laser sources emitting in the visible region of the spectrum. This means that the scattered Raman radiation can pass efficiently through, and be focussed by, the glass lenses. The major advantage of the microscope is that any sample or part of a sample that can be apertured optically can also have the Raman spectrum recorded. The theoretical spatial resolution is  $\sim 1\text{ }\mu\text{m}$ . Clearly this will be dependent on the wavelength of the laser source, and the NIR 1064 nm lasers with microscope attached have a theoretical spatial resolution of  $\sim 5\text{ }\mu\text{m}$ . This is clearly a case of having to decide whether spatial resolution or fluorescence is the bigger issue. The high spatial resolution, and the use of automated stages, enables mapping and imaging experiments to be carried out relatively easily. However there are disadvantages. For example, obtaining a representative spectrum from a film, which may at the microscopic level be inhomogeneous, is difficult. Further, obtaining the spectrum from any significant volume of a solution by detecting a microscopic volume may not be the most effective arrangement. However, if the microscope is an integral part of the instrument, it is possible to buy a small adaptor, which enables collection from a larger volume. These essentially consist of a device which screws into the microscope holder and has a mirror which turns the beam  $90^\circ$  to the microscope direction. A 1 cm cuvette or spinning sample holder can then be mounted on the edge of the microscope stage.

From the optical engineer's point of view, the use of a microscope to detect the scattering has some advantages. A relatively low-powered laser can be used since it will be focussed to give a very small spot giving a high power density at the sample and also a large collection angle. Further, the small excitation volume can be efficiently imaged into a small spectrometer and onto the detector. The microscope can be set up as a simple microscope or can be set up confocally. The advantages of using a microscope have so far focussed only on the  $X$ - $Y$  plane. The microscope can also be used to advantage by changing the focus in the  $Z$  direction. In the confocal arrangement, the microscope contains a pinhole in its focal plane, which enables only light focussed on the plane containing the sample to be collected efficiently. The pinhole filter stops most other light since it is not focussed sharply in the plane of the pinhole. An alternative system is adopted on some instruments. In this, a slit is placed in the focal plane of the microscope at right angles to the slit of the spectrometer. In this way, the two slits although well separated in the instrument are crossed to create essentially a pinhole. In either case the intention is to discriminate against light, which may arise from anywhere other than from the spot sharply focussed on the sample.

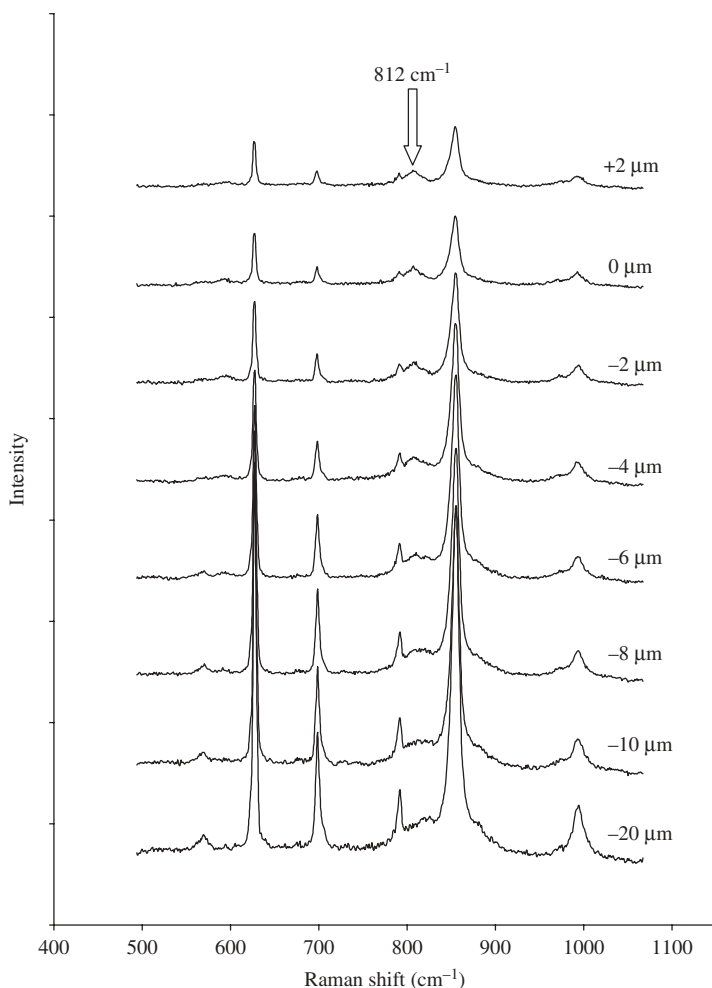
### **2.7.1 Depth Profiling**

With this arrangement, it is possible to obtain some depth profiling of the material. The microscope is focussed at different depths into the sample and the

spectra recorded at each depth. From a knowledge of the magnification of the microscope objective used, it is then possible to work out the volume excited and consequently the position in the sample from which the spectra was obtained. Although this would seem in principle relatively simple, there is a considerable problem created by refraction [24, 25] as the beam enters the other material which in general will have a different dielectric constant from that of the air between the sample and the microscope. This can be decreased to some extent by using water immersion and oil immersion objectives, but in general considerable care must be taken when estimating the true depth into the sample. However, given this limitation it is still possible to obtain some information about how a signal changes with depth in the sample. A depth profile taken with a microscope with 632 nm excitation for the polymer polyethylene terephthalate is shown in Figure 2.17.

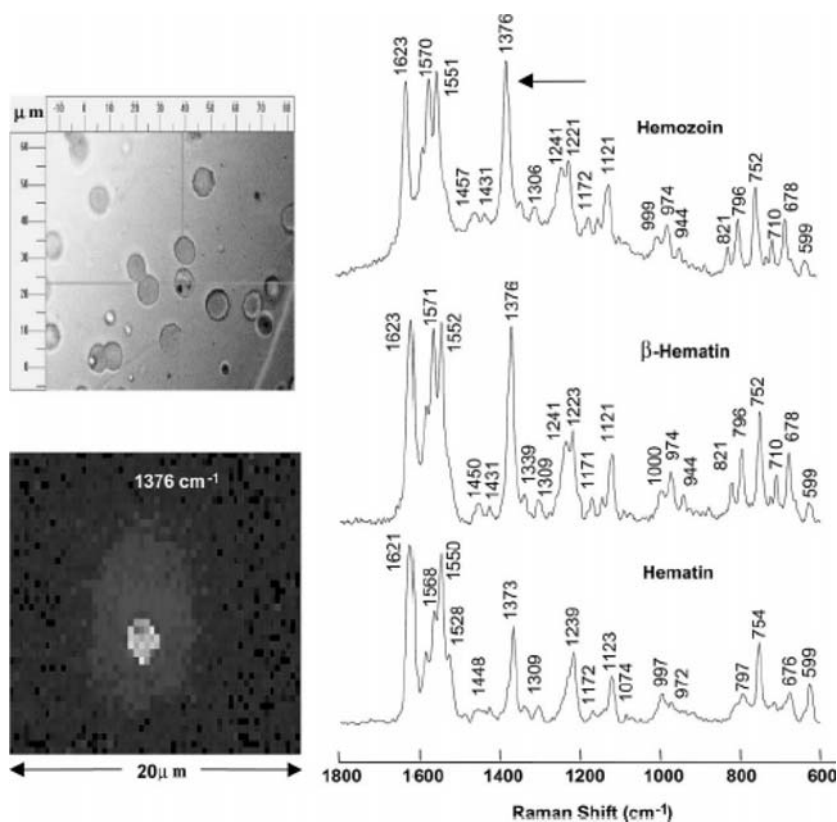
### 2.7.2 Imaging and Mapping

The techniques of Raman mapping and imaging arise from the use of microscopy with Raman spectrometers. The CCD devices used as detectors are essentially similar chips to those used in digital cameras and camcorders. They are arranged in an array of pixels each of which can be individually addressed. The difference in Raman scattering is that, since the signal is weak, the background noise is critically important and consequently in most instruments, the sample is cooled using three-stage Peltier cooling or even liquid nitrogen cooling. Some less expensive spectrometers employ standard chips used in cameras either with no cooling or with single-stage cooling. In the normal arrangement, the scattered light is separated into individual frequencies in the monochromator and focussed as a line on the CCD so that each separate frequency can be detected at a different point along the line. An alternative way of collecting Raman scattering is that instead of using a monochromator to split up the different frequencies, a set of filters can be used, in a manner analogous to that used by Raman in the initial experiment. In this arrangement only light of a particular frequency range corresponding to the frequency of one of the major vibrations of the molecule to be detected can pass through to the detector. In this arrangement, there is no monochromator to split up the light and the detector operates exactly like a camera recording an image of the sample focussed under the microscope. The only difference is that only light of the frequency of the Raman active vibration can reach the detector so a Raman image is recorded. This is called imaging. Figure 2.18 shows a combination of effects [26]. The photomicrograph and corresponding Raman image of the  $1374\text{ cm}^{-1}$  band clearly shows a parasite's food vacuole along with the spectra of hemozoin, L-hematin and hematin all acquired using 780 nm excitation. The spectrum of hemozoin is identical to the spectrum of L-hematin at all applied excitation wavelengths. The band enhancement of  $A_{1g}$  modes, explained in



**Figure 2.17.** Confocal depth profile of 78  $\mu\text{m}$  acrylic latex coated on 200  $\mu\text{m}$  PET coating. The depth resolution was determined to be 4  $\mu\text{m}$  with a  $\times 50$  objective at 632.8 nm. Spectra were collected from the coating surface (0  $\mu\text{m}$ ) and at 2  $\mu\text{m}$  intervals through the polymer (spectra labelled -2  $\mu\text{m}$  through to -20  $\mu\text{m}$ ). The uppermost spectrum was collected when the laser beam was focussed 2  $\mu\text{m}$  above the coating surface, so that the Raman scattering arose from the residual, or defocused, part of the beam. (Reproduced with permission from G.D. Macanally, N.J. Everall, J.M. Chalmers and W.E. Smith, *Applied Spectroscopy*, **57**, 44 (2003).)

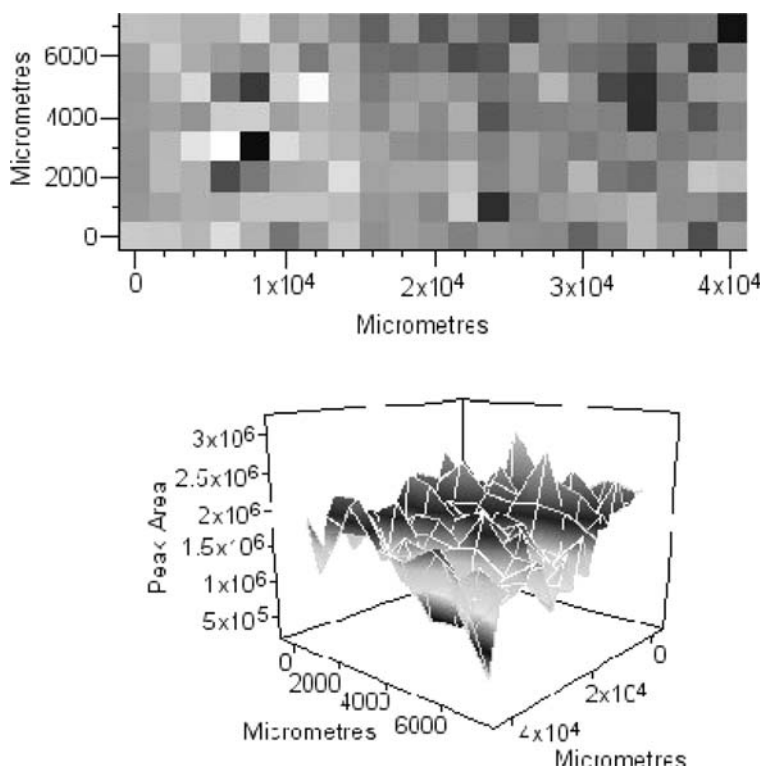
Chapter 4, including X4 (1374  $\text{cm}^{-1}$ ) enables Raman imaging of hemozoin in the food vacuole. This enhancement, resulting from excitonic coupling between linked porphyrin moieties in the extended porphyrin array, enables the investigation of hemozoin within its natural environment.



**Figure 2.18.** Raman imaging. Photomicrograph and corresponding Raman image of the  $1374\text{ cm}^{-1}$  band. (Reprinted from B.R. Wood, S.J. Langford, B.M. Cooke, F.K. Glenister, J. Lim and D. McNaughton, *FEBS Letters*, **554**, 247–252 (2003).)

An alternative method is to map the surface. Accurate positional devices are now readily obtainable and using a suitable XYZ device, it is possible to use the standard configuration to take a Raman spectrum from a small area, move the sample so that the next small area is under the microscope and take another spectrum. By doing this repeatedly, spectra from a selected area can be obtained. From this data, any one vibration can be selected and a map of the intensity variation for that vibration plotted. Figure 2.19 shows typical maps. One is a black and white image of the surface with each pixel shown being a point at which a spectrum was taken. The lighter the pixel, the more intense the Raman scattering recorded. The other map shows a 3D representation. These maps were obtained from a surface in which a number of small particles, which give extremely strong Raman signals, had been deposited. The position of the particles can clearly be seen from the peaks shown in the map.





**Figure 2.19.** Raman maps – pixel map (top); 3D map (bottom). (Reproduced with permission from A. McCabe, W.E. Smith, G. Thomson, D. Batchelder, R. Lacey, G. Ashcroft and B. Fulger, *Applied Spectroscopy*, **56**, 820 (2002).)

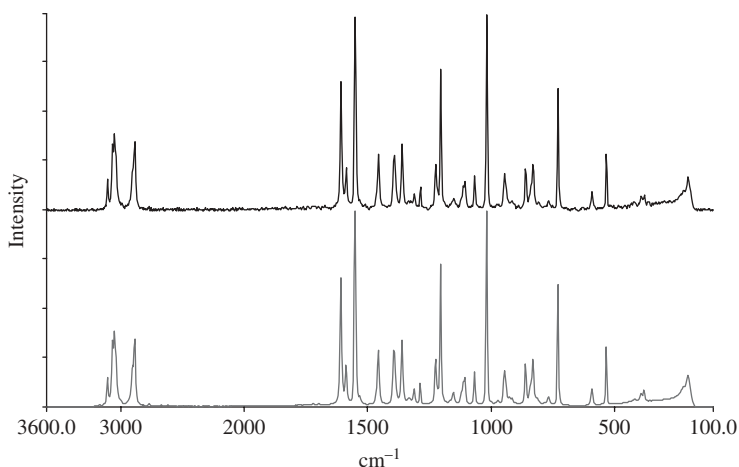
Imaging has the advantage that it is rapid but the disadvantages that only one particular region of the spectra can be surveyed at one time and the resolution is limited. Mapping has the advantage that the whole spectrum is recorded and stored on the computer. A map of all vibrations observed could be obtained if required. However, it is very slow in practice. Obtaining Raman spectra by either of these techniques but in particular by mapping has large advantages in that the material can be immediately identified from the spectrum information obtained and its distribution in a heterogeneous sample determined. One use of this technique has been to study the distribution of drugs in tablets by mapping the surface. This identifies not only the drug but also other components such as fillers and binders and gives their distribution. Apart from the value of this information in formulation, distribution in a tablet is difficult to counterfeit. The best maps of this type can take days to complete.

## 2.8 CALIBRATION

So far we have considered the spectrometer components and sample presentation. Before continuing to examine and manipulate the data, a question which should regularly be asked is, 'How do you know that your instrument is working correctly and consistently?' It is a question being asked of industrial spectroscopists more and more, specifically by regulatory authorities. As Raman spectroscopy is growing in industrial use, the questions are being rightly asked by non-scientists. The pharmaceutical industry, in particular, have to register new products before sale to the public. The regulators wish to know that the measurements have been made correctly, on correctly working instruments which will give the 'same' answer today and tomorrow on the 'same' or similar samples. The question is particularly important if quantitative work is carried out. Apart from regulatory requirements, industrial spectroscopists often require quantitative methods to be transferred between instruments. This is a topic in which interest has recently increased particularly in NIST and ASTM. The search for a simple standard and method of calibration continues but at least one daily check has been published by McCreery [27].

Most of the checks that are carried out are to ensure that the  $x$ -axis or wavenumber position is correct. The phrase 'calibration' is often used but that is not possible for most spectroscopists; it can be done only by engineers. The checks that are carried out are better described as performance checks. Barium sulphate has a strong band at  $988\text{ cm}^{-1}$ , diamond a band at  $1364\text{ cm}^{-1}$  and silicon a band at  $520\text{ cm}^{-1}$  which are now used by some instrument manufacturers. In addition, indene [28], cyclohexane and sulphur have well-known band positions as measured on dispersive instruments. However calibrating relative peak heights is a rarely mentioned field. For NIR FT Raman spectrometers the situation is worse. Whilst the sulphur spectrum maintains relative band strengths, indene bands vary greatly in relative intensity with laser power (Figure 2.20).

Whilst the spectra appear very similar, the ratio of the  $2890$  to  $1550\text{ cm}^{-1}$  bands does not change linearly with a change in laser power from 10 to 350 mW. A number of compounds with absorption bands in the NIR spectrum above the laser line at  $1064\text{ nm}$  show this effect. This appears to particularly affect compounds with aliphatic hydrocarbon groups. The bands with a Raman shift of  $\sim 3000\text{ cm}^{-1}$  are actually scattered at a true frequency of  $6398\text{ cm}^{-1}$  which is equivalent to  $1562\text{ nm}$ . This is very close to the broad NIR aliphatic hydrocarbon overtone bands at approximately  $1666\text{ nm}$ , halogenated dienes have been suggested as a possible standard. The  $\nu\text{CH}$  bands, and others near to the limits of the detector range, are also frequently strongly attenuated compared to spectra excited with a visible light laser. Bands are likely to be severely attenuated when they occur close to the cut-off edges of the filter used to block the elastically scattered radiation occurring at the exciting line frequency. Recently, standards based on fluorophores have been proposed for spectrometers with visible laser sources.



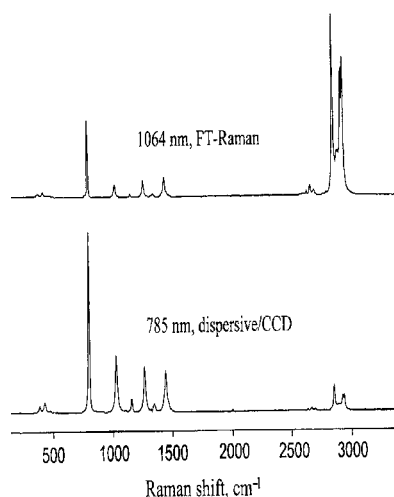
**Figure 2.20.** Indene at 1064 nm – 10 mw (top); 350 mw (bottom).

A neon lamp on the beam axis can provide a wavelength calibration standard. Halogenated dienes and cyclohexane have been suggested as possible Raman wavenumber standards [29]. The latter does have a variable spectrum dependent on the wavelength of the laser source used. The spectrum has to be corrected for instrument response as shown in Figure 2.21.

An ASTM standard (ASTM E 1840) has now been established for calibrating the Raman shift axis. Eight common chemicals – 1,4-bis(2-methylstyryl) benzene, naphthalene, sulphur, 50/50(v/v)toluene/acetonitrile, 4-acetamidophenol, benzonitrile, cyclohexane and polystyrene had the Raman spectra recorded by six different laboratories using both dispersive and FT spectrometers. Apart from a few of the values at high and low frequencies, standard deviations of  $<1\text{ cm}^{-1}$  were reported.

The instrument response is variable across the  $x$ -axis. Using tungsten lamps is often quoted as the way to measure instrument response. Unfortunately the lamp energy is dependent on temperature and this varies with the lifetime of the bulb. For an accurate calibration, the filament temperature would have to be measured. The use of tungsten lamps and glass filters has been proposed by NIST [30] and adopted by instrument manufacturers [31] to overcome this issue, particularly for transfer of quantitative methods. To calibrate the  $y$ -axis, a simple, practical calibration standard for instrument response correction, based on the use of luminescent standards (fluorophores), was proposed [32]. These have been developed further by using correction polynomials. These are available via the Internet [33].

Whilst standards are now becoming more available, there is still not a universal, easy to use, sample which calibrates both wavenumber and intensity



**Figure 2.21.** Cyclohexane uncorrected for instrument response. (Reproduced from Richard L. McCreery, *Raman Spectroscopy for Chemical Analysis*, John Wiley & Sons, Inc., New York, 2000.)

in a single spectrum. The luminescent standards have to be used in the same sampling geometry as the sample of interest. The wavenumbers position can be affected by several instrument features particularly in FT systems [34].

## 2.9 DATA HANDLING, MANIPULATION AND QUANTITATION

Having organized the Raman experiment with regard to sample presentation and instrument operation, we need to consider how the data will be generated and manipulated. The latter will depend on the use to which the data is put. As already stated, the phrase ‘interpretation of vibrational spectra’ is used in many different ways. In a qualitative way the spectrum of a molecule can be the subject of a full mathematical interpretation in which every band is carefully assigned or of a cursory look to produce the interpretation ‘Yes that is acetone’. Alternatively the spectra could be employed to monitor or determine composition in a quantitative way. Whichever way the data is used, the manipulation which has occurred during production has to be considered.

### 2.9.1 Production of Spectra

Raman instruments are single-beam instruments that are operated in the vast majority of cases without the need for a background reference spectrum. The

nature of the spectra produced can be affected both by the Raman instrumentation and by the way in which the data is manipulated following collection. However instrumental features such as filters or beam splitters can affect the spectrum. Dispersive instruments may employ more than one filter or monochromator to cover a wide spectral range. At the change over point energy difference can affect the band strengths although this is less of a problem as modern instruments. In FT spectrometers the raw data is not a spectrum but an interferogram. This is computer manipulated before presentation as a spectrum.

The relative strengths of the bands in the  $3000\text{ cm}^{-1}$  region are particularly affected in FT Raman and as discussed above the use of 792 or 850 nm excitation with visible Raman systems can also affect relative intensities. Perhaps the biggest feature is the direction of polarization of the laser beam but this will be discussed in Chapter 3. Background correction of spectra can be carried out with a white light source. In the ideal world this would have a known, invariable temperature. In practice this does vary with time and can cause variations in the background as can a change of filters, etc. These effects are most critical for quantitative measurements rather than qualitative measurements. The effects of apodization and resolution can be seen in the spectra from FT Raman instruments. A major advantage and also a problem with modern instruments is the flexibility of the software used following data capture.

Before digital displays were commonly used, if the spectrum was weak, this was instantly obvious. Now it is easy to produce an apparently strong spectrum by simply changing the intensity scale. This is often carried out automatically by the instrument. If care is not taken to read the *Y* scale, the information that the spectrum is weak can be missed. A weak spectrum may be due to too little sample, poor preparation, the fact that the 'sample' is loaded with a diluent such as salt or simply that the sample is a poor Raman scatterer. In the last case, the spectrum may be from an impurity due to a strong Raman scatterer in the sample matrix. Further, spectra are often scaled for comparison with each other by overlaying. This is usually carried out by choosing a band common to both spectra. The experienced spectroscopist will look at the noise present on the spectra away from the main peaks to judge the relative intensity at the peaks of the spectra in their original form. However, modern programmes also contain smoothing routines which on many occasions can be quite useful. In this case, the smoothing routine can be used to remove all noise from the spectra and prevent an estimate of intensity.

Spectra can be subjected to manipulation by expansion, smoothing, baseline flattening, spectral subtraction and numerous other software programs, not forgetting the effects of the apodization function in the FT instruments. Once the initial spectrum has been produced, any further software manipulation or enhancement should be approached with great care. In many cases the

manipulation can make the spectrum look pretty but will result in the loss of vital information for interpretation. These routines should only be used with an understanding of what may be occurring!

Perhaps the most dangerous feature of spectrum manipulation is overuse of smoothing programmes. They can often be used to make very small features of the spectra into large looking features by selecting the spectral range recorded and smoothing out any noise present in the spectrum to obtain a smooth looking band, which gives the impression it is a major feature. The fact that the band is a minor feature does not make it unimportant. It may well be extremely important. It does however increase the possibility that it arises from an impurity or other spurious cause in the spectrum. Overall however, if used correctly, these modern data handling programmes are extremely effective.

### **2.9.2 Display of Spectra**

Spectral presentation is generally not an issue. Raman spectra are usually presented as just the Stokes spectra with the anti-Stokes spectra omitted. The only inconsistent feature is in the way in which the wavelength scale is displayed, sometimes from high to low wavenumber but often from low to high wavenumber. There are semantic debates as to which is correct. Purists say that all graphical scales should be displayed with the lowest value at the origin. Others say that the wavelength scale, in Raman spectrometers, is a shift and not an absolute measurement. For comparison with infrared spectra, the high to low format is preferred. In this format both infrared and Raman spectra from the same sample can be overlaid and band positions compared. All bands in a Raman spectrum rise from a baseline against a linear scale. This scale varies from instrument to instrument and cannot be easily used for direct quantitative measurements. They can be used for comparative measurements and band ratio quantitation.

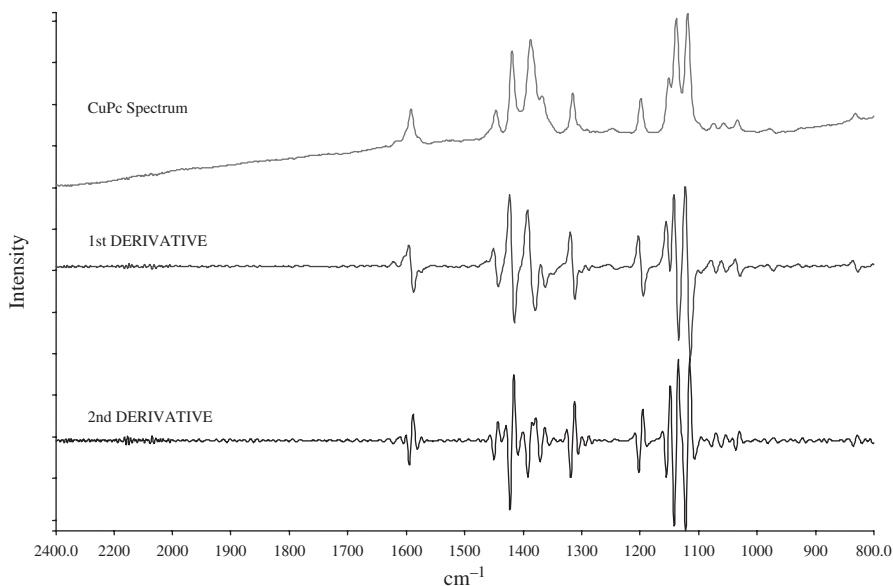
#### **□ SPECTRUM SCALES**

Modern instruments almost invariably produce spectra which fill the screen or the page of a printout. Two spectra can be given equal importance if careful observation is not made of the intensity scale. Data systems automatically scale spectra so that the strongest peak is that which stretches to the top of the screen. By ignoring this effect information about the sample can be lost. As previously stated, a weak spectrum can be due to instrument effects, sample mounting, diluents or the sample having a low Raman scatter cross-section. If spectra of samples from different points in a matrix appear to be of the same strength, just because of scale expansion important information can be lost or misinterpreted.

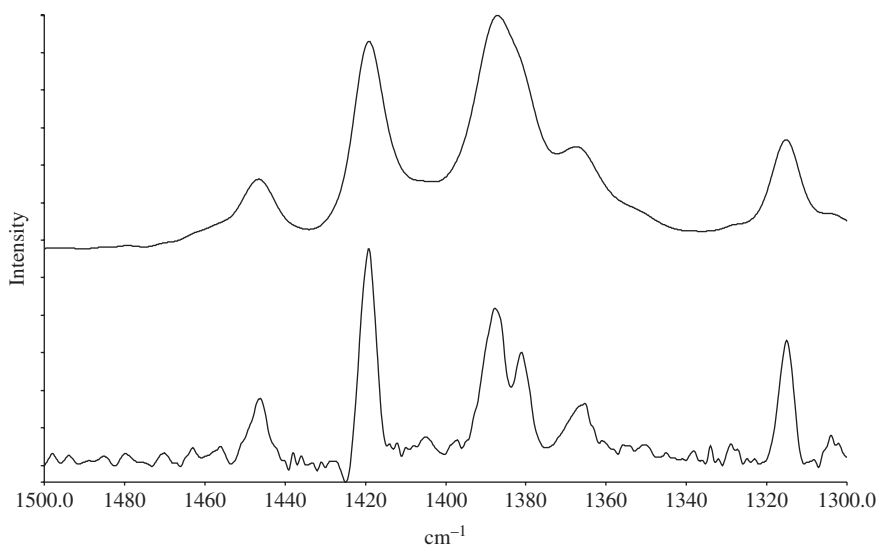
A legitimate way to scale spectra for comparison purposes is normalising. This is usually carried out by adding a standard or choosing a band common to both spectra. The absorbance of the band in the strongest spectrum is fixed and the same band in the comparison spectrum scaled to fit. Other bands in the spectra are scaled but the relative intensities to the main band remain the same.

#### □ SPECTRAL ENHANCEMENT/LOSS OF DATA

A number of data handling packages available for manipulating spectra are meant to enhance the appearance of the spectrum, particularly for inclusion in reports or publications. Although many claim to improve, or facilitate, interpretation, if not used with great care the opposite effect can be achieved. Software packages are available which will reduce or remove the slope from all or part of the spectrum. This can be very useful to Raman spectroscopists to remove fluorescence backgrounds, but could lead to wrong assumptions on purity or affect quantitative measurements. If quantitative work is being carried out, another way of correcting for a background slope is to carry out derivative spectroscopy. As can be seen in Figure 2.22 the spectrum of the second derivative has a flat baseline but identifying individual bands can be complex.



**Figure 2.22.** Derivative Raman spectra.



**Figure 2.23.** Deconvolution of Raman bands from a broad spectrum.

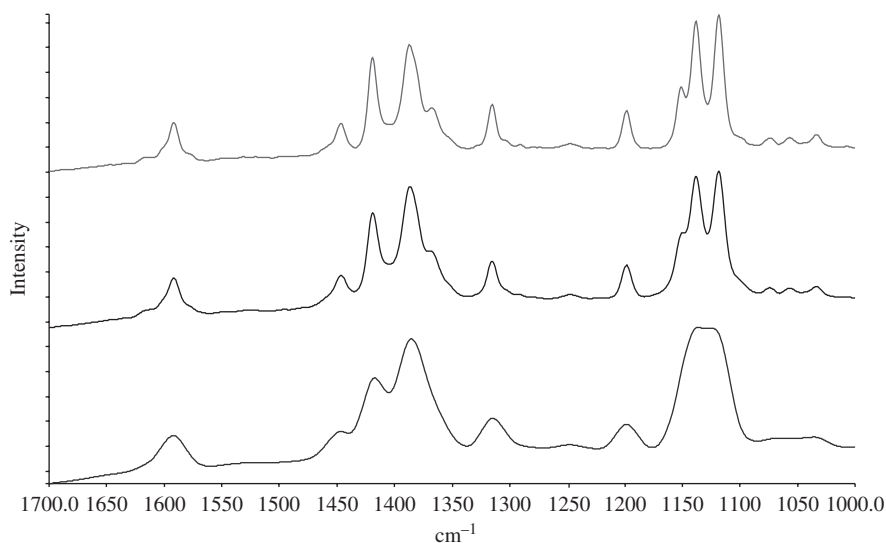
Many data systems contain routines to produce peaks from within a broad envelope as can be seen in Figure 2.23. These are referred to as deconvolution routines. These are often useful for quantitative studies when the number of components is known. Good judgement has to be made as to when to stop if the number of components is unknown. In the latter case information is not lost as much as spurious bands are produced. An example of these routines being used effectively is given in Chapter 4 (Figure 4.9).

The SMOOTH function is one which can be used as a precision tool to enhance a spectrum or a blunt instrument to totally destroy it. If a spectrum has a low signal to noise ratio, the effects of the noise can be reduced with a light smooth to make the bands appear more clearly. A heavy smooth can not only lose shoulders, but remove some bands completely. Figure 2.24 shows a noisy spectrum with several degrees of smooth.

### 2.9.3 Quantitation

The data handling procedures have concentrated on the effects on the qualitative aspects of the spectrum, but vibrational spectroscopy is also used quantitatively. For most uses of Raman scattering, the essential feature is the ability to detect the spectrum. The frequency values are given with reasonable accuracy. Intensities, on the other hand, are usually treated as relative intensities or described as 'strong', 'medium' and 'weak'. This is sufficient information if what is required is to use the spectrum as a fingerprint for the molecule or





**Figure 2.24.** Smoothed Raman spectra with the foot spectrum showing the danger of over smoothing.

molecules from which the scattering occurs. On normal infrared laboratory instruments, quantitative analysis is carried out either by measuring the absorbance of a specific band or by ratioing the absorbances of component specific bands. As Raman spectroscopy employs a scattering technique, the absolute band intensity is dependent on a number of factors such as orientation, laser power and other instrumental effects which cannot be reliably reproduced. Until recently absolute band intensity measurements ought to have been avoided. Advances in instrumentation and stability are starting to open up this area of application. Relative strength determinations can be made, in multi-component samples, by measuring the ratio of intensities of relative bands. However the relative Raman scattering cross-section should be borne in mind for each component. The calibration curves should ideally be constructed from similar samples of known composition. For more than two components, synthetic mixtures do not usually provide adequate calibration curves. Real samples can contain minor components which contribute to band shape and size. Components may also interact with each other and solvents to produce variations in peak position, shape and size. As already mentioned, particle size, self-absorption and depolarization ratios can all affect relative band strengths.

Bands may be measured in various ways. The most common method is peak height. A baseline point must be established which takes account of band shape, neighbouring bands and possible fluorescence. The absolute position of the base point is not critical but the method of determining the point must be

consistent in the calibration and test samples. All the spectrometer conditions, sample concentrations, sampling volume and, where relevant, cell window material or reflection angles must be noted, if the measurement is to be repeated or transferred to different instruments. Relative band intensities will vary with different wavelength laser sources as there is  $\sim \nu^4$  dependency on signal intensity with absolute wavenumber. As already mentioned self-absorption can affect band intensities, particularly in NIR Raman. Relative intensities can also be enhanced by resonance as described in Chapters 4 and 5. Temperature may also be critical in some measurements, especially at high laser power or with a strongly absorbing sample which could under go thermal degradation.

Raman spectroscopy carried out in most experiments is not an absolute quantitative method but mainly comparative. However, quantitative information can be obtained from single peaks with the relevant data treatment and careful consideration of the factors which may affect the result. These fall into two categories – those which affect production of the data, being hardware- or sample-related and those which occur during data handling.

#### □ QUANTITATION – HARDWARE AND SAMPLING FEATURES

All Raman spectrometers are essentially single beam instruments and consequently any quantitative analysis procedure will be dependent on the stability of the laser and the detector. Further, the same instrumental condition will require to be used on each occasion the analysis is carried out. It is unlikely that this can be done without significant fluctuation due to changes, for example, in laser power with time. As a result, all quantitative measurements using Raman scattering should make use of a calibrant which should be run at the same time and preferably interspersed with the samples used in the quantitative procedure. All the spectrometer conditions, sample concentrations, sampling volume and, where relevant, cell window material or reflection angles must be noted, if the measurement is to be repeated or transferred to different instruments. Temperature may also be critical in some measurements.

One problem is that the flexibility of Raman sampling can mean that reproducibly replacing a sample may be difficult. The use of focussed beams in Raman scattering to obtain higher power means that relatively small volumes of solution are usually interrogated. For example, although a 1 cm cuvette is used, the volume of the sample within the cuvette actually sampled is usually of the order of microlitres. To obtain effective Raman scattering from this volume, the beam must first of all pass through the holder and therefore be refracted by it and then through the media. The scattered radiation then repeats the process on the way back to the detector. The depth at which the sample is focussed can alter the signal, and any mis-alignment of the cell which causes a slight displacement of the laser beam can also affect signal intensity. Thus, it is

essential that a stable holder is built which defines the position of the sample in relation to the collection optics. It is also essential that the instrument parameters be set in exactly the same position on each occasion. If this is done, and provided a statistically large enough number of spectra are taken per sample and regular standards are included in each set of measurements, effective quantitation can be obtained. The standards used should span the wavelength range of the peaks measured in the analyte. The use of a silicon standard with a peak at about  $550\text{ cm}^{-1}$  with an organic sample for which the main peaks are in the region  $1000\text{--}1600\text{ cm}^{-1}$  is poor practice. In principle, the instrument should cope with the difference in frequency, but the authors have obtained changes caused on one occasion by a slipping stage on a grating in the instrument and in another with the use of near-infrared radiation with a visible system where the detection of the Raman lines was close to the edge of the range for the detector. This caused differential changes in the relative intensities of the bands depending on frequency.

As with other optical techniques, it is easier to quantify solutions or gases rather than solids where the nature of the solid can have a large effect on the spectra obtained. The use of the micro sampler attached to a microscope, or the use of a system without a microscope, so that a representatively large amount of the solution is detected is also a help. Examples of the use of Raman for quantitation are given in Chapter 5.

Clearly, a double beam approach would be more effective for quantitation. However, many modern UV visible spectrometers designed for quantitative use no longer have the double beam arrangement. One possible approach is to use a cell split into two with one half filled with sample and the other with the standard. The cell is spun so that the standard and sample spectra are recorded regularly over a period of time. The result is then obtained from the average accumulated signal. However, these can be difficult to fill and to use. The reliability of modern machines is sufficiently good not to need to do this. The most important variable to check is the laser power which if not automatically compensated can drift considerably over a day. Recently, instruments which can record quantitative spectra in the standard 96 or 384 well-microtitre plates widely used in biology have become available.

## □ QUANTITATION – DATA HANDLING CONSIDERATIONS

The intensity from which quantitation is to be obtained can be measured in various ways. The most common method is to measure the height of a major peak, but peak area can sometimes be a better measurement. At some point in the spectra, a baseline which shows no Raman scattering must be established; this should take account of band shape and neighbouring bands. The absolute position of the base point is not critical but the method of determining the point

must be consistent in the calibration and test samples. As with the qualitative manipulations, there are a large number of quantitative software packages available. Some can be used for composition analyses which attempt a simple least squares fit, through principle component regression (PCR) to partial least squares (PLS) modelling. Besides these, spectral enhancement and band resolution packages are available on many instruments. Simple derivative spectroscopy has already been mentioned, but Fourier domain processing and curve fitting routines, sometimes in complex combinations, can also be employed. All must be employed with an understanding of the applicability of the package used to the problem being studied. Otherwise the result can be due more to the imaginative component than the real.

A number of texts delve deeply into the mathematics of the quantitative aspects of vibrational spectroscopy. We have only highlighted here the features which are of particular note for Raman spectroscopists.

## **2.10 APPROACH TO QUALITATIVE INTERPRETATION**

In Chapter 1 the basic theory of and approach to interpreting a Raman spectrum were set out. In this chapter we have considered various instrument features such as the source wavelength, accessories which give effective sampling and how data production can affect the final spectrum. All these factors should be borne in mind before any attempt is made to interpret a spectrum. In fact some of these parameters may have been specifically chosen to enhance a particular feature of interest. In Raman spectroscopy whole techniques can be devoted to specific enhancement as will be seen with the SERRS effect in Chapter 5. If the basic structure of a molecule is known, then the theory expounded in Chapters 1, 3, 4 and 5 will assist the spectroscopist to make great progress towards gaining chemical, physical and even electronic information about the state of the molecule. Subtle and not so subtle changes in bands can yield extensive specific information about the molecule. Vibrational spectroscopy is often used in attempts to identify unknown materials, to characterise reaction by-products and to follow reactions. Raman spectroscopy in this context is a poor cousin of infrared spectroscopy and to some extent has been oversold. It should be noted that although Raman spectra are often simpler and clearer than infrared spectra, they can be less easy to fingerprint since some groups do not give strong bands and there are far fewer published, recorded reference spectra for direct comparison with unknowns. However, like most tools when used with skill and the correct approach, Raman spectroscopy can be of great assistance in identifying unknown materials or components. To do this successfully the maximum information about the sample should be obtained and borne in mind during the analysis and it is essential to be aware of problems which can lead to an erroneous result.

### 2.10.1 Factors to Consider in the Interpretation of a Raman Spectrum of an Unknown Sample

In a practical interpretation it is essential that all available information is used and that the possibility of contamination is considered. There are a number of examples in the literature of this simple precaution being ignored and important conclusions drawn on data which subsequently were shown to have arisen from a contaminant. Whilst in both Raman and infrared spectroscopy, interpretation of the spectrum requires knowledge of all the factors which may be affecting the spectrum, Raman spectroscopy has fewer complexities. Sample preparation is often zero with samples being examined as neat solids, liquids or gases, with only a few possible artefacts. Some instrumental effects such as cosmic rays and emission from room lights and in particular strip lights and cathode ray tubes can show up in the spectrum. These appear abnormally strong in weak spectra where scale expansion has been used. Some but not all of these features can be recognized because the bandwidth is narrow but it is essential that thorough checks are made for the presence of these peaks.

It is important not to lose sight of the overall picture. If simple information on the nature of the sample is ignored, answers can be generated which common sense tells us are impossible. The very different intensities of Raman scattering from various vibrations from different molecules in a matrix can easily lead to this sort of wrong interpretation. A polymer bottle may contain sulphur. Polymers are weak scatterers whereas sulphur is a strong scatterer. The fact that the spectrum is dominated by the sulphur peak does not mean that the polymer is largely sulphur. This is a rather trivial example but this mistake is easy to make when two organic molecules are present in a matrix.

Raman spectra are not obviously dependent on the chemical and physical environment of the sample being examined. Whether the molecules are in a gaseous, liquid, solid or polymeric form is not easily apparent from the spectrum, but the physical state does affect the overall strength and band shape. In general, crystalline solids give sharp, strong spectra whilst liquids and vapours tend to have much weaker spectra. Pressure, orientation, crystal size, perfection and polymorphism may affect the spectra, but the changes can be subtle. Raman spectra are however particularly temperature-sensitive. Broad bands in Raman spectra tend to be due to fluorescence, burning, low resolution or weak bands that have been enhanced, e.g. from glass or water. Chemical groups may also respond to hydrogen bonding and pH changes but these changes tend to be shown in peak shifts rather than changes in band shape.

So having recorded the spectrum, we need to develop an approach which will help as much as possible towards solving the problem. By sequentially going through the next steps the chances of making an error in interpretation will be much reduced but success is not guaranteed!

## □ KNOWLEDGE OF THE SAMPLE

A lot of information can be gained by understanding the way in which a sample arrived in the state presented for examination. The analyst should consider the following questions. How was the sample produced? What is known of the reaction scheme? Are there possible side reactions? Could solvents be present? Did work-up conditions introduce impurities? What was the type of equipment the sample came from? (Grease, drum linings, coupling tubes and filter aids can all appear in or as the sample spectrum.)

Solids – Is it ‘dry’, or a paste? Has it been washed with a solvent or re-crystallized?

Liquids – Are they volatile, are they alkaline, neutral or acidic?

Vapours – What temperatures/pressures are involved?

How pure is the sample thought to be? Is any elemental information available, does the sample contain N, S, or halogens? Could these come from an impurity?

Are there likely polarization, orientation or temperature effects?

The answers to these questions are not always available but these points should be kept in mind if the spectrum does not appear as expected. The spectrum of a sample without any known history or source should be approached with great care. Something is always known even if it is only physical form and colour.

## □ SAMPLE PREPARATION EFFECTS

Handling the sample may affect the resultant spectrum; as mentioned in previous sections, the information required may dictate the sample preparation and/or presentation method. Knowing the method should provide some information about a sample but beware.

- Solids – Is it neat, a halide disk or mull? If it is a mull, mark off any bands from the mulling agent. Is the sample a neat powder, could this produce orientation or particle size effects? If the sample has been diluted because it has a strong colour why say it is a colourless material?
- Is the sample in a container? Mark off the bands due to the vessel walls, e.g. glass, polythene.
- In cast or polymer films, is there any solvent trapped or encapsulated? Can polymer films have orientation?
- Liquids – Is the sample a pure liquid or a solution? If the latter, mark the solvent bands.
- Microscopy – Are the bands real, or due to the mounting window, e.g. diamond?

## ❑ INSTRUMENT/SOFTWARE EFFECTS

The above-mentioned approach checks that all the bands and overall shape of the spectrum are not affected by the samples and the method of preparation; however, extra bands and anomalies may occur from instrument or software artefacts.

- Which laser line is used as a source, are resonance or self-absorption likely to affect band strengths?
- Does the spectrum really have a flat background or has a software background correction removed fluorescence, and destroyed information?
- Is the spectrum as strong as it appears? Check the scale and check for expansion routines.
- Has a smooth function been applied which leads to loss of bands normally resolved?
- Modern data systems display and plot information on data manipulation. Has this been applied? The lack of printed information does not mean manipulation has not occurred.
- Are the broad bands in the Raman spectrum due to fluorescence or burning?
- Are these sharp bands in the Raman spectrum which could come from cosmic rays or neon room lights?

## ❑ THE SPECTRUM

Once all the information on the sample history is acquired, and all possible distortions and artefacts have been identified, or dismissed, interpretation of the band positions and strengths should begin.

- Look at the total spectrum as a picture, does it look as expected from the sample. Are the bands broad or sharp? Are they strong or weak? Is the background sloping or flat? If it appears correct continue with band position interpretation.
- Start at the high wavenumber end, in the  $3600\text{--}3100\text{ cm}^{-1}$  region; are there any  $\text{--OH}$  or  $\text{--NH}$  bands? Refer to Tables 1.1–1.5 to determine the type, and for confirmation, look for related bands in other parts of the spectrum, e.g. amides have carbonyl bands as well as  $\text{--NH}$  bands. These bands can be weak in Raman spectra and are easily missed or not seen.
- In the  $3200\text{--}2700\text{ cm}^{-1}$  region, are there unsaturation or aliphatic bands present? Unsaturation is usually above  $3000\text{ cm}^{-1}$ , aliphatics below. If aliphatic bands are present, are they largely methyl or longer  $\text{--CH}_2\text{--}$  groups? Again refer to the tables for confirmation by other bands.
- Are these bands in the cumulative bond (e.g.  $\text{--N=C=N--}$ ) region  $2700\text{--}2000\text{ cm}^{-1}$ ?

- Are these bands in the double bond (e.g.  $\text{C}=\text{O}$ ,  $\text{C}=\text{C}$ ) region  $1800\text{--}1600\text{ cm}^{-1}$ ? In the Raman spectrum unsaturated double bond bands are generally stronger and sharper than carbonyl bands. Infrared active bands can also appear in this region.
- By these checks, it should be established if the spectrum contains aliphatic, unsaturated or aromatic groups. Multiple bond bands or carbonyl bands should also have been identified. Look at the rest of the spectrum for strong bands. Do they correspond to bands in the tables?
- The region below  $1600\text{ cm}^{-1}$  contains many bands largely due to the fingerprint of the molecule. Structural information can be gained from this region, but bands are mainly due to the backbone of the molecule. Selected phenyl ring modes and groups such as the azo group can be identified. Other groups with bands in this region tend to be oxygenated organics, e.g. nitro, sulpho, or heavily halogenated hydrocarbons. Inorganics have sharp Raman bands in this region (see tables in Chapter 6).
- Besides information identifying groups, is there negative information from bands that are not present? If the  $3200\text{--}2700\text{ cm}^{-1}$  region contains only very weak or no bands, then this negative information could be due to unusual species such as the halogenated species mentioned, that the Raman bands of these groups are too weak or that the sample is inorganic.
- Having established the possible groups present in the spectrum, can they be combined into a molecule which can be expected from the known chemistry and/or from the knowledge of possible impurities?

Always, wherever possible, crosscheck the interpretation by visibly matching to a reference spectrum of the molecule or of a very similar structure. Never trust peak list or computer search printouts without visually matching the spectra.

Finally check again if the answer makes sense with the sample. Is a red powder really ethanol? If this general procedure is followed, then the maximum information will be obtained from the examination, and errors will be minimized.

## 2.10.2 Computer Aided Spectrum Interpretation

Raman spectra can be interpreted for identification of substances by pattern matching, either by computer or by the hard work of visually searching through hard copy reference collections. There are now many commercial software packages and libraries available for rapid database searching of infrared spectra but still relatively few for Raman spectra. If computer searching is used, 'answers' must be crosschecked by visually comparing the sample and reference spectra. Do not rely on lists of nearest hits. Spectra can also be interpreted from first principles, by determining the chemical structural groups present from significant band positions, as stated previously. However, this type of interpretation is very difficult with Raman spectra. A knowledge of the type of chemistry involved is



often a useful aid. Interpretation of spectra often requires experience and an understanding of the relevant answer required, particularly when mixtures or impure samples are examined.

Computer aided spectrum interpretation can be generally divided into two types. The most common is library searching or pattern matching. The other is structural elucidation, which is sometimes part of a training package or library search package for infrared spectra but is rarely found for Raman spectra.

#### □ LIBRARY SEARCH SYSTEMS

Most Raman instrument manufacturers now offer their own library search routines which contain a few pre-recorded reference spectra and can be expanded with the user's own recorded spectra. Several can be enhanced with electronic versions of hard copy libraries such as the Aldrich and Sadtler<sup>TM</sup> collections. The major library publishing companies also offer their own versions of electronic libraries as standalone library search systems. There is growth in Internet searchable libraries but Raman spectra are still very sparse.

#### □ STRUCTURAL DETERMINATION AIDS

There have been many attempts at the development of artificial intelligence or expert systems to emulate the human thought process for spectral interpretation. Most have been successful for a limited range of similar chemical compounds or structures, but none have yet approached the full range attempted by humans. Many manufacturers of various spectroscopic instruments are including software training packages in their range of offerings, which very graphically demonstrate the fundamental principles of interpretation. Several now include excellent 3D graphic representation of band origins with simultaneous twisting, bending and stretching of bonds. These usually work very well for a limited range or group of molecules, but cannot be added to by the spectroscopist. As stated before Raman spectra are rarely included in this type of package.

An opposite approach is to use packages for DFT calculations to predict the band positions of various groups in the Raman spectrum of a molecule. These packages now can predict spectra which are very close to the spectra of actual samples. However it must be remembered that these packages generally assume single molecules in the vapour phase. Recorded spectra of solids and liquids can have band shifts due to molecular interactions.

#### □ SPECTRA FORMATS FOR TRANSFER AND EXCHANGE OF DATA

Vibrational spectroscopists very quickly realized the potential of computers to manipulate spectra for quantitative or qualitative work. However this initially required using software supplied by the instrument manufacturer or difficult

and tedious manipulation of the spectra files for transfer to another computer. With the advent of PC workstations and the establishment of large commercial databases, the demand grew for a universal format for data transfer. In 1987 the Joint Committee on Atomic and Molecular Physical Properties (JCAMP) proposed a format to be used internationally. This is known as JCAMP-DX. The format was intended to represent all data in a series of labelled ASCII fields of variable length. Very quickly the major instrument manufacturers provided software to convert their spectra to/from JCAMP format. Unfortunately whilst the data format was clearly specified, the file header format was less tightly specified. As a result commas, spaces, etc., were used in different ways as delimiters. The effect was that each manufacturer supplied a slightly different JCAMP file. A number of commercial spectrum file converters are now available which allow for the import and export of files from most spectrometers into data handling packages. The proliferation of Windows<sup>TM</sup> based software has also removed the need for file transfer as the image of a spectrum can easily be transferred into reports and presentations using 'cut and paste' techniques.

## □ THE INTERNET

We are beginning to see what could become an explosion in the use of the Internet for spectroscopic information and assistance. All of the main instrument manufacturers have established home pages on the Internet. These are mainly used for promotional material but many have plans to provide access to notes on applications and give details of training courses or seminars. Most hard copy journals on spectroscopy are now available on the Internet for a fee. The *Society for Applied Spectroscopy (SAS)* journal has free monthly article listings. Recent editions have articles available in abstract form; however, the page numbers are not listed. Advance notices of meetings and events are also available. The *Internet Journal of Vibrational Spectroscopy* is free. It is a source of 'how to do it' articles, as well as the more formal journal articles. It contains a long list of links to relevant Internet sources. The free internet journal *Spectroscopy Now* has a specific Raman page.

## 2.11 SUMMARY

The advantages and disadvantages of Raman spectroscopy from a practical viewpoint are very clear from what is said in this chapter. It is extremely flexible and can be configured in many different ways. The continued improvements in modern optics including small diode lasers, improved simple detectors and fibre optic coupling have all led to the ability to use Raman scattering for problems for which we would not previously have considered it. Since it is a non-contact technique, it is possible to use it in a chemical factory with dust or inside the

head of a combustion engine. Although the technique is limited by the fact that it is a weak effect, to some extent this can be overcome where the power density is high by the use of a microscope or particular forms of fibre optics. Thus, the future of Raman spectroscopy would appear to be set to advance particularly for specific analysis purposes. The disadvantage this creates is that the range of choice requires an understanding of the subject and cannot be made simply on the basis of the purchase of one simple instrument. However, most laboratories find that modern Raman instrumentation – visible or near-infrared FT systems – can solve many of the standard problems for which Raman scattering is deemed to be a suitable technique.

## REFERENCES

1. P. Hendra, C. Jones and G. Warnes, *FT Raman Spectroscopy*, Ellis Horwood Ltd, Chichester, 1991.
2. B.T. Bowie, D.B. Chase and P. Griffiths, *Appl. Spectrosc.*, **54**, 200–207A (2000).
3. M.V. Pellow-Jarman, P.J. Hendra and R.J. Lehnert, *Vib. Spectrosc.*, **12**, 257–261 (1996).
4. H. Wang, C.K. Mann and J.V. Vickers, *Appl. Spectrosc.*, **56**, 1538–1544 (2002).
5. C.H. Chio, S.K. Sharma, P.G. Lucey and D.W. Muenow, *Appl. Spectrosc.*, **57**, 774–783 (2003).
6. B. Schrader and G.Z. Bergmann, *Anal. Chem.*, **225**, 230–247 (1967).
7. P.J. Hendra, *IJVS*, **1**, edition 1, section 1 ([www.ijvs.com](http://www.ijvs.com)).
8. G. Dent, *Spectrochim. Acta A*, **51**, 1975 (1995).
9. Y.D. West, *IJVS*, **1**, edition 1, section 1 ([www.ijvs.com](http://www.ijvs.com)).
10. K.J. Asselin and B. Chase, *Appl. Spectrosc.*, **48**, 699 (1994).
11. G. Dent and F. Farrell, *Spectrochim. Acta A*, **53**, 21–23 (1997).
12. C. Petty, *Vib. Spectrosc.*, **2**, 263 (1991).
13. N. Everall, *J. Raman Spectrosc.*, **25**, 813–819 (1994).
14. N. Everall and J. Lumsdon, *Vib. Spectrosc.*, **2**, 257–261 (1991).
15. J.S. Church, A.S. Davie, D.W. James, W.-H. Leong and D.J. Tucker, *Appl. Spectrosc.*, **48**(7), 813–817 (1994).
16. D. Loudon, in: *Laboratory Methods in Vibrational Spectroscopy*, H.A. Willis, J.H. van der Mass and R.J. Miller (eds), John Wiley & Sons, Inc., New York, 1987.
17. M. Fleischmann, P.J. Hendra and A.J. McQuillan, *Chem. Phys. Lett.*, **26**, 163 (1974).
18. J.R. Lewis and P.R. Griffiths, *Appl. Spectrosc.*, **50**, 12A (1996).
19. S.M. Angel, T.F. Cooney and H. Trey Skinner, in: *Modern Techniques in Raman Spectroscopy*, J.J. Laserna (ed.), Ch. 10, John Wiley & Sons, Inc., New York, 2000.
20. D.A. Smith, S. Webster, M. Ayad, S.D. Evans, D. Fogherty and D. Batchelder, *Ultramicroscopy*, **61**, 247–252 (1995).
21. L. Song, S. Liu, V. Zhelyaskov and M.A. El-Sayed, *Appl. Spectrosc.*, **52**, 1364 (1998).
22. S.D. Schwab and R.L. McCreery, *Appl. Spectrosc.*, **41**, 126 (1987).

23. W. Xu, S. Xu, Z. Lu, L. Chen, B. Zhao and Y. Ozaki, *Appl. Spectrosc.*, **58**, 414–419 (2004).
24. N.J. Everall, *Appl. Spectrosc.*, **54**, 1515–1520 (2000).
25. N.J. Everall, *Appl. Spectrosc.*, **54**, 773–782 (2000).
26. B.R. Wood, S.J. Langford, B.M. Cooke, F.K. Glenister, J. Lim and D. McNaughton, *FEBS Lett.*, **554**, 247–252 (2003).
27. R.L. McCreery, *Raman Spectroscopy for Chemical Analysis*, Ch. 10, John Wiley & Sons, Inc., New York, 2000.
28. D.A. Carter, W.R. Thompson, C.E. Taylor and J.E. Pemberton, *Appl. Spectrosc.*, **49**, 11 (1995).
29. A.W. Fountain III, C.K. Mann and T.J. Vickers, *Appl. Spectrosc.*, **49**, 1048–1053 (1995).
30. NIST, [www.cstl.nist.gov/div837/Division/techac/2000/RamanStandards.htm](http://www.cstl.nist.gov/div837/Division/techac/2000/RamanStandards.htm).
31. Kayser, [www.kosi.com/raman/product/accessories/hca.html](http://www.kosi.com/raman/product/accessories/hca.html).
32. K.G. Ray and R.L. McCreery, *Appl. Spectrosc.*, **51**(1), 108–116 (1997).
33. R.L. McCreery, [www.chemistry.ohio-state.edu/~rmccreer/intensity/intensity.html](http://www.chemistry.ohio-state.edu/~rmccreer/intensity/intensity.html).
34. B.T. Bowie, D.B. Chase and P. Griffiths, *Appl. Spectrosc.*, **54**, 164–173A (2000).

## BIBLIOGRAPHY

This chapter contains a number of instructions and comments in sample preparation and use of accessories. These are not prescriptive, but based on experience, including getting it wrong. Sample specific and local needs will determine optimal conditions and procedures. To reference each original or milestone publication, invention, or application would have been too daunting a task; many have been gradually developed and improved by numerous workers over many years. Occasional references are given in the text to point the reader to greater in-depth understanding of the principles behind some of the necessarily brief descriptions. In addition to these, a short recommended bibliography relevant to this chapter is given.

- J. Chalmers and P. Griffiths (eds), *Handbook of Vibrational Spectroscopy*, Vols 1 and 2, John Wiley & Sons, Inc., New York, 2001.
- D.J. Gardiner and P.R. Graves (eds), *Practical Raman Spectroscopy*, Springer-Verlag, Berlin, Heidelberg, 1989.
- J.G. Grasselli and B.J. Bulkin (eds), *Analytical Raman Spectroscopy*, John Wiley & Sons, Inc., New York, 1991.
- ASTM, *1995 Annual Book of ASTM STDs, Vol. 3.06*, ASTM Philadelphia. (Designation E1683–95 Standard Practice For Testing the Performance of Scanning Raman Spectrometers.)

## SOFTWARE INTERPRETATION TOOLS, DATABASES AND INTERNET SITES

Charles B. Adams, Colombia University, *IR Tutor*.  
Biorad Laboratories, Sadtler Division, *IR Mentor*, *HaveIT all + new database*.

Chemical Concepts *Specinfo* Spectral Databases and *SpecTool* + new database.  
*Internet Journal of Vibrational Spectroscopy* (<http://www.ijvs.com>).  
*Society for Applied Spectroscopy* (<http://www.s-a-s.org/journal/journal.htm>).  
*Spectrochimica Acta* (<http://www.chemweb.com/gateways/elsevier.html>).  
*Spectroscopy Europe* (<http://www.spectroscopyeurope.com>).  
*Vibrational Spectroscopy* (<http://www.chemweb.com/gateways/elsevier.html>).  
*Chemscape CHIME* (<http://www.mdli.co.uk/downloads/downloadable/index.jsp>).  
Raman Shift Frequency Standards (ASTME 1848) (<http://chemistry.ohio-state.edu/~rmccreer/shift.html#shiftdir>).

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# Chapter 3

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## The Theory of Raman Spectroscopy

### 3.1 INTRODUCTION

As shown in Chapter 1, the sharp pattern of bands which make up a Raman spectrum makes it possible to use the technique for many types of analysis without a deep understanding of the nature of the effect. For example, it is possible to identify a molecule *in situ* from the pattern of bands and it may even be possible to determine the amount of the compound which is present. However a better understanding of the theory has real advantages. Much more information about a molecule and its surroundings can be obtained, the interpretation will be more secure, more possible pitfalls will be recognized and avoided, and the background required to understand some of the more exciting modern developments will be understood. There are many more detailed books on the theory of Raman spectroscopy but this chapter sets out and explains the salient points required for a more in-depth understanding. For example, where a mathematical treatment is required to make a specific point, the key equations are explained without a full derivation. The reader is referred to [1, 2] for a more thorough coverage.

Historically, Raman scattering has been described both in terms of ‘classical theory’ and ‘quantum theory’. The older classical theory is based on the wave theory of light and is deficient in that it does not take into account the quantized nature of vibrations. In addition it is not able to explain as much about the relationship between molecular properties and Raman scattering as quantum theory. Thus, although this theory has persisted as an approach in many books, it is not described further here. Accounts of the theory can be obtained in [1, 2].

### 3.2 ABSORPTION AND SCATTERING

When light interacts with matter, it can be absorbed or scattered. The process of absorption, discussed briefly in Chapter 1, requires that the energy of the incident photon corresponds to the energy gap between the ground state of a molecule and the excited state. It is the basic process used in a wide range of spectroscopic techniques and will be familiar to many readers. In contrast, scattering can occur whether or not there is a suitable pair of energy levels to absorb the radiation, and the interaction between the light and the molecule which causes this requires a different approach.

When a light wave, considered as a propagating oscillating dipole, passes over a molecule, it can interact and distort the cloud of electrons round the nuclei. This energy is released in the form of scattered radiation. Consider first the relative sizes of a light wave and a molecule. In the visible region, the wavelength of the light is between 400 and 700 nm whereas the size of a small molecule such as carbon tetrachloride is about 0.3–0.4 nm. Thus the oscillating dipole is much larger than the molecule. If it interacts with the molecule as it passes, it causes the electrons to polarize and go to a higher energy state. At that instant, the energy present in the light wave is transferred into the molecule. This interaction can be considered as the formation of a very short-lived ‘complex’ between the light energy and the electrons in the molecule in which the nuclei do not have time to move appreciably. This results in a high energy form of the molecule with a different electron geometry but without any large nuclear movement. This ‘complex’ between the light and the molecule is not stable and the light is released immediately as scattered radiation. It is often called the virtual state of the molecule. Since it has a different electronic geometry from that found in the static molecule and the nuclei do not have time to respond and reach a new equilibrium geometry to fit the distorted electronic arrangement, none of the electronic states of the molecule will describe the electron arrangement. Further the actual shape of the distorted electron arrangement will depend on how much energy is transferred to the molecule and hence is dependent on the frequency of the laser used. Thus, the laser defines the energy of the virtual state and the extent of the distortion. This virtual state is a real state of the transitory ‘complex’ formed.

The process differs from an absorption process in a number of ways. Firstly, the additional energy does not promote an electron to any one excited state of the static molecule; all states of the static molecule are involved to different extents and are mixed together to form states of the distorted ‘complex’. The energy of this state is dependent on the energy of the laser used and the amount of distortion is dependent on the electronic properties of the molecule and on the energy of the laser. Secondly, the lifetime of the excited state is very short compared to most absorption processes. The radiation is scattered as a sphere

and not lost by energy transfer within the molecule or emitted at a lower energy. Thirdly, and this will be dealt with later in this chapter, there is a link between the polarization of the exciting and scattered photons which can be of value in assigning particular vibrations.

Two types of scattering are readily identified. The most intense form of scattering, Rayleigh scattering, occurs when the electron cloud relaxes without any nuclear movement. This is essentially an elastic process and there is no appreciable change in energy. Raman scattering on the other hand is a much rarer event which involves only one in  $10^6$ – $10^8$  of the photons scattered. This occurs when the light and the electrons interact and the nuclei begin to move at the same time. Since the nuclei are much heavier than the electrons, there is an appreciable change in energy of the molecule to either lower or higher energy depending on whether the process starts with a molecule in the ground state (Stokes scattering) or from a molecule in a vibrationally excited state (anti-Stokes scattering). Figure 1.2 in Chapter 1 shows a simple diagram illustrating Rayleigh and Raman scattering. In each case the energy of the virtual state is defined by the energy of the incoming laser. The two states marked  $m$  and  $n$  are different vibrational states of the ground electronic state.

Most molecules at rest prior to interaction with the laser and at room temperature are likely to be in the ground vibrational state. Therefore the majority of Raman scattering will be Stokes Raman scattering. The ratio of the intensities of the Stokes and anti-Stokes scattering is dependent on the number of molecules in the ground and excited vibrational levels. This can be calculated from the Boltzmann equation,

$$\frac{N_n}{N_m} = \frac{g_n}{g_m} \exp \left[ \frac{-(E_n - E_m)}{kT} \right] \quad (3.1)$$

$N_n$  is the number of molecules in the excited vibrational energy level ( $n$ ),  
 $N_m$  is the number of molecules in the ground vibrational energy level ( $m$ ),  
 $g$  is the degeneracy of the levels  $n$  and  $m$ ,  
 $E_n - E_m$  is the difference in energy between the vibrational energy levels,  
 $k$  is Boltzmann's constant ( $1.3807 \times 10^{-23} \text{ JK}^{-1}$ ).

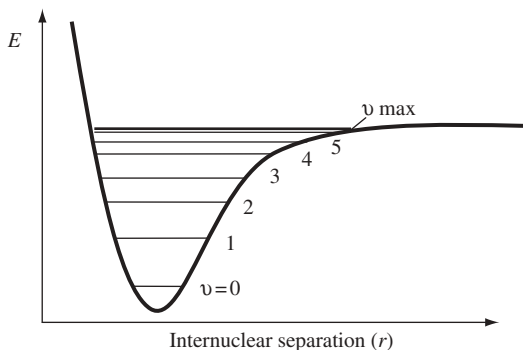
We shall see, when we consider symmetry later in this chapter, that some vibrations can occur in more than one way and the energies of the different ways are the same, so that the individual components cannot be separately identified. The number of these components is called the degeneracy and is given the symbol  $g$  in Equation (3.1). Since the Boltzmann distribution has to take into account all possible vibrational states, we have to correct for this. For most states  $g$  will equal 1 but for degenerate vibrations it can equal 2 or 3.



### 3.3 STATES OF A SYSTEM AND HOOKE'S LAW

Any molecule consists of a series of electronic states each of which contains a large number of vibrational and rotational states. In Figure 3.1 a sketch of a typical ground electronic state of a molecule is shown. The  $y$ -axis represents the energy of the system and the  $x$ -axis the internuclear separation. The curved line represents the electronic state. At large internuclear separations, the atoms are essentially free and as the distance decreases they are attracted to each other to form a bond. If they approach too closely, the nuclear forces cause repulsion and the energy of the molecule rises steeply as shown. Thus the lowest energy is at the bond length. However within the curve, not every energy is possible since the molecules will be vibrating and the vibrational energies, which are quantized, have to be taken into account. The tie lines are the quantized vibrational states. A particular vibrational level of a particular electronic state is often called a vibronic level.

At first glance this curve, referred to as a Morse curve, is relatively simple but there are more complications which are generally not added because the diagram gets too cluttered for use. What is shown in the figure refers to one vibration. The first level ( $v = 0$ ) is the ground state where the molecule is not vibrating and the second level ( $v = 1$ ) is the state where one quantum of the correct energy is absorbed and the molecule vibrates. The levels above this require energies of approximately but not exactly two times, three times, four times, etc., of the quanta required to move the molecule from the ground state 0 to the first excited state 1. Where a change of more than one quantum occurs the peak obtained is called an overtone. As we shall see, in Raman scattering this occurs only in special circumstances. In most Raman spectra overtones are predicted as very weak or non-existent. To describe all the vibrations in a molecule such as in Figure 3.1, a similar set of tie lines but at different energies



**Figure 3.1.** A typical Morse curve for an electronic state showing the vibrational levels as horizontal tie lines.

is required for each vibration. Further, vibrations can combine so that one quantum of one vibration and one of another vibration will give a new level. In the spectrum, peaks due to these combinations are called combination bands and like overtones appear only in certain circumstances. To make matters even more complicated, rotational levels, which are of lower energy than vibrational levels, also require to be added. A diagram with all these levels is too complex to use and conventionally is simplified either by showing all the levels for one vibration or one vibrational level for each vibration depending on the use to which the diagram will be put.

To describe the process of absorption when an electron is excited from one electronic state to another, a Morse curve for the ground and excited state is required with the excited state plotted above the ground state since it will be at higher energy. In Raman scattering, as we shall see later in the chapter, all excited vibronic states have an influence on scattering efficiency. As a result, in principle, we require to draw Morse curves for all states of the molecule. However, the influence of each state is not specific and hence a simpler diagram as shown in Figure 1.2 can be used in which all the many excited vibronic levels from the many excited electronic states are represented by a few lines. Further, since Raman scattering is fast compared to the time for nuclear movement, there is no appreciable change in the nuclear separation during any one scattering event and therefore no change along the  $x$ -axis. Thus, for a simple description of the process, energy changes in the molecule are plotted as vertical lines and states as horizontal lines with the other features of the Morse curve neglected.

By way of revision, it is useful to remind ourselves of the main features of Figure 1.2. It shows the energy changes which occur when the exciting radiation interacts with the molecule to form a 'virtual' state and the scattering which follows when the molecule relaxes. The scattered radiation is what we measure as Raman scattering and the energy difference between the excitation and scattering processes corresponds to the energy of vibrations of the molecule. As we shall see below, the two levels can vary by only one quantum number for fundamentals. There are features in Figure 1.2 which are potentially misleading. The  $y$ -axis is an energy axis. However, in Raman scattering the energy of a C=C vibration may typically be between 1600 and 1000  $\text{cm}^{-1}$  but the energy of a green laser will be about 20,000  $\text{cm}^{-1}$ . Very often, as here, the energy of the laser radiation is not given accurately because the desire is to show the vibration spacing clearly, and plotting the true excitation energy would lead to a very large separation between the ground state and the virtual state reducing the space to show the vibronic levels.

The shape of the Morse curve makes it difficult, but not impossible, to calculate the energy of vibronic levels and so simple theory uses the harmonic approximation. In this approach, the Morse curve shown is replaced by a parabola calculated for a diatomic molecule by considering it as two masses connected by a vibrating spring.

With this approach, Hooke's law (Equation (3.2)) gives the relationship between frequency, the mass of the atoms involved in the vibration and the bond strength for a diatomic molecule:

$$\nu = \frac{1}{2\pi c} \sqrt{\frac{K}{\mu}} \quad (3.2)$$

where  $c$  is the velocity of light,  $K$  is the force constant of the bond between A and B, and  $\mu$  is the reduced mass of atoms A and B of masses  $M_A$  and  $M_B$ :

$$\mu = \frac{M_A M_B}{M_A + M_B} \quad (3.3)$$

Hooke's law makes it easy to understand the approximate order of the energies of specific vibrations. The lighter the atoms, the higher the frequency will be. Thus C–H vibrations lie just below and just above  $3000\text{ cm}^{-1}$  and C–I vibrations at less than  $500\text{ cm}^{-1}$ . The force constant is a measure of bond strength. The stronger the bond, the higher the frequency will be. A list of vibrational energies is given in Chapter 1.

Two other points should be noted. The harmonic approximation predicts that the overtones of a molecule are equally spaced but the reality is that the departure from harmonicity in a real system will mean that, particularly at higher energies, the energy separations between levels will decrease. For example, in Figure 3.1 which shows a Morse curve for one vibration, all the vibrational levels are shown as they actually are, with a decreased separation in energy the higher the vibrational quantum number. They would be shown equally spaced in the harmonic approximation. Further, the electron density along the vibration is of importance in working out the efficiency of the Raman process. We will make use of this later in discussing resonance in Chapter 4.

### 3.4 THE NATURE OF POLARIZABILITY AND THE MEASUREMENT OF POLARIZATION

When radiation is emitted from a source, a number of photons are emitted and each photon consists of an oscillating dipole. Observed at  $90^\circ$  to the direction of propagation, the beam looks like a wave. Observed looking along the line between the observer and the light source, each photon will appear as a line, with the oscillating dipole in that line. In general the angle of the line to the observer is random, but by passing the light through a suitable optical element such as a Nichol prism or a piece of Polaroid film, all the lines can be made to

propagate in one direction. This is called plane or linearly polarized radiation. The lasers that are normally used for excitation in Raman scattering are usually at least partially polarized. Good Raman spectrometers also have an optical element, a polarizer, that can be put in the beam to ensure that the light is linearly polarized.

When linearly polarized light interacts with the molecule, the electron cloud is distorted by an amount that depends on the ability of the electrons to polarize (i.e. the polarizability,  $\alpha$ ). The light causing the effect is polarized in one plane, but the effect on the electron cloud is in all directions. This can be described as a dipole change in the molecule in each of the three Cartesian co-ordinates  $x$ ,  $y$  and  $z$ . Thus, to describe the effect on molecular polarizability of an interaction with linearly polarized radiation, three dipoles require to be considered. The simple expression is that a dipole  $\mu$  is created in the molecule by the field from the incident photon  $E$ .

$$\mu = \alpha E \quad (3.4)$$

To allow for the polarization angle of the linearly polarized light, the polarizability components of the molecule are usually labelled, an example of which is shown below:

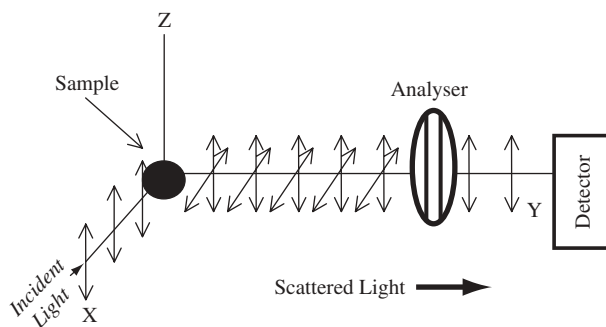
$$\alpha_{xx}$$

The first subscript  $x$  refers to the direction of polarisability of the molecule, and the second  $x$  refers to the polarization of the incident light. Thus,  $\mu_x = \alpha_{xx}E_x + \alpha_{xy}E_y + \alpha_{xz}E_z$ . Similar expressions will exist for both  $\mu_y$  and  $\mu_z$ .

Thus, the polarizability of the molecule is a tensor,

$$\begin{bmatrix} \mu_x \\ \mu_y \\ \mu_z \end{bmatrix} = \begin{bmatrix} \alpha_{xx} & \alpha_{xy} & \alpha_{xz} \\ \alpha_{yx} & \alpha_{yy} & \alpha_{yz} \\ \alpha_{zx} & \alpha_{zy} & \alpha_{zz} \end{bmatrix} \begin{bmatrix} E_x \\ E_y \\ E_z \end{bmatrix}$$

There are specific advantages of this rather complex arrangement. In Raman scattering the incident and scattered beams are related. If radiation of a particular polarization is used to create the Raman scattering, the polarization of the scattered beam is related to but not necessarily the same as that of the incident beam. Thus, a Raman spectrometer has an optical element, the polarizer, to control the polarization of the incident beam. It ensures that the radiation is plane polarized and determines the angle of the plane of the incident radiation. A second element, the analyser, analyses the polarization of the scattered beam. The analyser works by allowing the polarized light to pass through to the detector only in one plane. It is initially set to allow transmission of scattered radiation in the plane of the incident radiation (called



**Figure 3.2.** Arrangement to monitor polarization of Raman scattering. The arrows indicate the plane of the scattered light. The analysis is set to allow through only parallel scattering. If rotated  $90^\circ$  it will allow through only perpendicular scattering.

parallel scattering). It is then set at  $90^\circ$  to this direction to allow any light in which the polarization direction has been changed by the molecule to pass through to reach the detector (called perpendicular scattering). This arrangement is shown in Figure 3.2.

If a single crystal is used as a sample, all molecular axes are lined up within the unit cell in the same direction for each cell. Thus, the polarization direction of the incident radiation bears a relationship to the molecular axes. With an arrangement like this, it is possible to analyse each of the components of the tensor shown above. This works best for crystals in higher symmetry space groups but not cubic. Light is a dipole property, which means that the optical axes of a material are set at  $90^\circ$  to each other. In some higher symmetry space groups such as the tetragonal space group, the optical and crystal axes are at right angles and so they can be aligned to match the polarization direction of the incident beam. Under these circumstances, light polarized in the  $z$  direction, passing through the crystal along the  $z$ -axis, will pick out the component  $\alpha_{zz}$ . In all likelihood there will be a molecular axis along the  $z$ -axis and so the information can be related to molecular properties. However in most situations the analysis is more complex. Light which is not sent down an axis of the crystal will rotate within it and in many crystal space groups, the crystal axes are not at right angles and bear a complex relationship to the molecular axes. Thus this approach is very informative for a very limited number of samples. It is not dealt with further here but the reader should be aware of the possibility that, when using single crystal samples, the intensities of the bands may be affected by the structure.

Often, the samples we examine are either in the gas phase or in solution. In either case there is no ordering of the axes of the molecule to the polarization direction of the light but information can still be obtained from polarization measurements. What is measured in practice is the depolarization ratio where

the intensity of a given peak is measured with the plane of polarization of the incident light parallel or perpendicular to the scattered light analysed. For samples such as this, it is useful to express the average polarizability in terms of two separate quantities that are invariant to rotation, namely isotropic and anisotropic scattering. Isotropic scattering is measured with the analyser parallel to the plane of the incident radiation and anisotropic scattering with the analyser perpendicular to the plane. It is possible to solve the tensor and calculate the ratio of parallel to perpendicular scattering (see [1]). This ratio is what is actually measured. It is called the depolarization ratio ( $\rho$ ). Here we illustrate the salient equations but do not give details since this ratio is usually used qualitatively and is often talked about but seldom calculated.

The isotropic and anisotropic parts of the tensor are represented in Equations (3.5) and (3.6),

$$\bar{\alpha} = \frac{1}{3}(\alpha_{xx} + \alpha_{yy} + \alpha_{zz}) \quad (3.5)$$

$$\gamma^2 = \frac{1}{2} \left[ (\alpha_{xx} - \alpha_{yy})^2 + (\alpha_{yy} - \alpha_{zz})^2 + (\alpha_{zz} - \alpha_{xx})^2 + 6(\alpha_{xy}^2 + \alpha_{xz}^2 + \alpha_{yz}^2) \right] \quad (3.6)$$

and the effect on parallel and perpendicular polarization of Equations (3.7) and (3.8),

$$\bar{\alpha}_{\parallel}^2 = \frac{1}{45} (45\bar{\alpha}^2 + 4\gamma^2) \quad (3.7)$$

$$\bar{\alpha}_{\perp}^2 = \frac{1}{15} \gamma^2 \quad (3.8)$$

This gives a ratio between parallel and perpendicular scattering as

$$\rho = \frac{\bar{\alpha}_{\perp}^2}{\bar{\alpha}_{\parallel}^2} = \frac{3\gamma^2}{45\bar{\alpha}^2 + 4\gamma^2} \quad (3.9)$$

The importance of this information becomes clear only when we consider the selection rules for Raman scattering later in the chapter. In essence, for a molecule with appreciable symmetry in solution or in the gas phase, the depolarization ratio varies depending on the symmetry of the vibration. Symmetric vibrations have the lowest depolarization ratios. Thus measurement of parallel and perpendicular scattering using the analyser to obtain the depolarization ratio provides a check on assignments of the peaks. This check is not available with absorption spectroscopies such as infrared.

There is one final practical point which has to be borne in mind. When radiation from the analyser is detected via a monochromator, the efficiency of the grating used to split up the light is dependent on the plane of polarization. This means the grating will transmit radiation to the detector more efficiently for either parallel or perpendicular polarization and consequently the apparent depolarization ratio will be wrong. The most conventional way to overcome this problem is to add an extra element, a scrambler, which scrambles the polarization of the light before it enters the monochromator so that the detector is equally efficient for all polarization directions of the incoming radiation. There are other ways of doing this. For example a half-wave plate can be inserted instead. This rotates the light by  $90^\circ$  and is swung into the beam in only one direction of the analyser so that the light in both analyser positions enters the monochromator in the same direction.

Failure to appreciate this effect can be serious. Laser radiation is usually linearly polarized to a significant extent. In the absence of polarizers and analysers and if no scrambler is in place, the laser acts as the polarizer and the monochromator as the analyser. This means that spectra often labelled as 'unpolarized' because no polarization optics were used will be polarized. As a result, the intensities can be misleading, particularly for molecules with high symmetry.

### **3.5 THE BASIC SELECTION RULE**

The basic selection rule is that Raman scattering arises from a change in polarizability in the molecule. As we shall demonstrate later, this means that symmetric vibrations will give the most intense Raman scattering. This is in complete contrast to infrared absorption where a dipole change in the molecule gives intensity and, at a very simple level, this means asymmetric rather than symmetric vibrations will be intense.

### **3.6 NUMBER AND SYMMETRY OF VIBRATIONS**

With any molecule, the energy can be divided into translational energy, vibrational energy and rotational energy. Translational energy can be described in terms of three vectors  $90^\circ$  to each other and so has three degrees of freedom. Rotational energy for most molecules can also be described in terms of three degrees of freedom. However, for a linear molecule there are only two rotations. The molecule can either rotate around the axis or about it. Thus, molecules are said to have three translational degrees of freedom and three rotational degrees of freedom with the exception of linear molecules, which have two degrees of rotational freedom. All other degrees of freedom will be

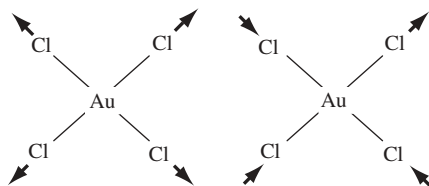
vibrational degrees of freedom and each is equivalent to one vibration. Therefore, the number of vibrations to be expected from a molecule with  $N$  atoms is  $3N - 6$  for all molecules except linear systems where it is  $3N - 5$ .

From this it is possible to work out the number of vibrations which occur. However, it must be noted that this does not make the vibrations either Raman or infrared active and in general we would not expect to observe all vibrations in either spectroscopy.

As discussed in Chapter 1, for a simple diatomic molecule, which by definition is linear, there is one vibration. For a simple homonuclear diatomic like oxygen or nitrogen this is a symmetric vibration in which we would not expect any infrared activity, but we would, since the bond is stretched, expect a change in polarizability to occur. Thus, one band would be expected in the Raman spectrum and there would be no band in the infrared spectrum.

When a molecule has a number of symmetry elements in its structure, more selection rules apply. Consider a square planar molecule such as  $\text{AuCl}_4^-$  which is illustrated with selected vibrational movements indicated by arrows in Figure 3.3. This molecule is said to have a centre of symmetry. The definition of a centre of symmetry is that any point in the molecule reflected through the central point will arrive at an identical point on the other side. Thus, in this molecule, ignoring vibrational movement, any chlorine atom reflected through the gold centre will arrive at an identical chlorine atom on the other side. An example of a molecule that does not possess this property is the nitrate ion in which an oxygen reflected through the nitrogen in the centre would arrive at a point in space (see Figure 3.4).

We need to have some way of describing the vibrations in a molecule. In principle, it would be possible to use  $x$ ,  $y$  and  $z$  co-ordinates and simply explain how each atom moves by how much these co-ordinates change. This would be complicated and we would not understand the nature of the information readily. The usual way is to use normal co-ordinates as shown for  $\text{AuCl}_4^-$  in Figure 3.3. Normal co-ordinates of a molecule make use of the natural directions of bonds and are those co-ordinates in which all atoms vibrating go through the centre of gravity of the molecule at the same time. The value of normal co-ordinates is that they provide a much better visual pattern of what a vibration looks like. Two vibrations for the  $\text{AuCl}_4^-$  molecule using normal co-ordinates are illustrated in Figure 3.3.



**Figure 3.3.** Illustration of two vibrations in the centrosymmetric ion  $\text{AuCl}_4^-$ .



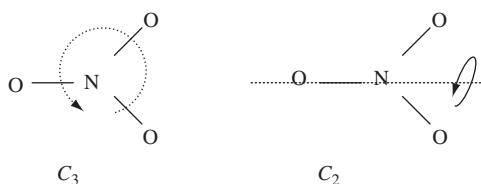
In one vibration, all the atoms move out at the same time, and in the other, two atoms move in as two move out. The arrows representing the movement of atoms could also be reflected through the centre in the same way as atoms. The assignment of the molecule as centrosymmetric was based on the properties of the atoms with the molecule at rest in its equilibrium position. The vibrational movements do not affect that. However, clearly there is a difference between the two vibrations as shown in Figure 3.3. For this reason, an extra label is used. Vibrations of the first type are called even, or gerade, and are labelled *g*, whereas those of the second type are odd, or ungerade, and are labelled *u*. This labelling applies only to molecules with a centre of symmetry. It will not, for example, apply in nitrate.

For any molecule with symmetry elements, it is possible to use symmetry to help understand molecular motion by applying group theory. The approach is very powerful in experiments involving molecules of high symmetry, and gives a better insight into selection rules. In addition, the use of labels which arise from group theory is common throughout the literature. To enable the reader to understand its value, the basics of the approach are described below. However, it is often not useful in experiments with more complex molecules and so an extensive treatment is outside of the scope of this book. Good texts such as the book by Cotton [3] describe the application of symmetry in detail.

### 3.7 SYMMETRY ELEMENTS AND POINT GROUPS

Any molecule can be classified by its symmetry elements (i.e. axes and planes). It is then possible to assign the molecule to a group called a point group which has these same elements. This can then be used to predict which bands are infrared and which are Raman active. To do this it is necessary to work out the symmetry elements in the molecule. The main symmetry elements we need to recognize are the following:

- E* – The identity element. This takes the molecule back into the same position it started from; i.e., a 360° rotation for every part of the molecule does this.
- C<sub>n</sub>* – An axis of symmetry in which the molecule is rotated about a molecular axis. *n* Defines how often the molecule requires to be rotated to arrive back at the starting point. Thus, in the nitrate ion shown in Figure 3.4, one possible axis is the one pointing straight out of the plane of the paper. If the molecule is rotated about it, each oxygen will require to be rotated three times to arrive back at the starting point. This is a *C<sub>3</sub>* axis. There may well be a number of axes in a molecule. For example in the nitrate ion, three *C<sub>2</sub>* axes also exist. They lie along the NO bonds and rotating the molecule about them would require two rotations to take the molecule back to its starting point. The axis with the highest value of *n*, for the nitrate *C<sub>3</sub>*, is known as the principle axis of the molecule.



**Figure 3.4.**  $C_3$  and  $C_2$  axes in the nitrate ion.

$\sigma_h$  – A plane of symmetry in which the plane is perpendicular to the principle axis of the molecule.

$\sigma_v$  – A plane of symmetry in which the plane is parallel to the principle axis of the molecule.

$i$  – A centre of inversion in which every point inverted through the centre arrives at an identical point on the other side.

$S_n$  – An axis which combines a rotation and an inversion.

These symmetry elements define a particular type of molecule. All molecules with the same set of symmetry elements are said to belong to the same point group.

To assign a molecule to its point group, the symmetry elements are first recognized and then analysed according to a set of rules. Usually symmetry elements are not analysed to assign a molecule to a particularly high symmetry point group such as the cubic point group, the octahedral point group and the tetrahedral point group. These can usually be recognized immediately. The questions we ask to make an assignment are set out in order below:

1. What is the principle axis of the molecule?
2. Is there a set of  $n$   $C_2$  axes at right angles to it? If the answer is no, carry on with the questions below. If the answer is yes, go to question 6.
3. Is there a plane perpendicular to the principle axis? If so, this is a  $\sigma_h$  plane. A molecule which has a  $C_n$  principle axis and a  $\sigma_h$  plane can be assigned to the point group  $C_{nh}$ .
4. If there is no  $\sigma_h$  plane, are there planes of symmetry parallel to the principle axis? There should be as many planes of symmetry as the  $n$  value. If this is the case, the point group is assigned as  $C_{nv}$ .
5. If there are no planes, the point group is assigned as  $C_n$ .
6. If the molecule has a principle axis and a set of  $n$   $C_2$  axes at right angles to it, is there a plane of symmetry perpendicular to the principle axis (i.e. a  $\sigma_h$  plane)? If this is the case, this molecule belongs to the  $D_{nh}$  point group.

7. If there is no  $\sigma_h$  plane of symmetry, is there a set of  $n$   $\sigma_v$  planes parallel to the principle axis? If the answer to this question is yes, then the point group is  $D_{nd}$ .
8. If there are no planes of symmetry, the molecule will belong to the  $D_n$  point group.

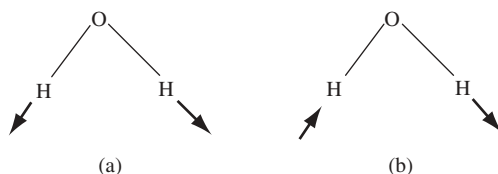
Other molecules will belong to lower symmetry point groups. For example, for some molecules there is an  $S_n$  axis or a  $\sigma_v$  plane or no symmetry element at all. These can be recognized and a point group assigned by inspection.

Having assigned the molecule to a point group, group theory can be used to predict whether or not a band will be Raman or infrared active. It is particularly important to note that symmetry considerations allow us to determine whether or not a band is allowed in a Raman or infrared spectrum. This does not tell us how strong it will be; this would require a calculation.

There is a group theory table for all point groups which defines the symmetry behaviour of every vibration of a molecule belonging to that point group. Below, we reproduce the  $C_{2v}$  point group table which would be the correct point group for a single molecule of water.

$C_{2v}$	$E$	$C_2$	$\sigma_v(xz)$	$\sigma'_v(yz)$		
$A_1$	1	1	1	1	$z$	$x^2, y^2, z^2$
$A_2$	1	1	-1	-1	$R_z$	$xy$
$B_1$	1	-1	1	-1	$x, R_y$	$xz$
$B_2$	1	-1	-1	1	$y, R_x$	$yz$

In the table, the symmetry elements are shown across the top. The first column contains a series of letters and numbers. The first one we see is  $A_1$ . This is a way of describing a vibration, or for that matter an electronic function. It describes what happens to the vibration with each symmetry element of the molecule. These symbols are called irreducible representations and the top line always contains the one which refers to the most symmetrical vibration in terms of its behaviour when it is rotated or reflected by the symmetry operations. In higher symmetry point groups where there is a centre of symmetry, there would also be a  $g$  or a  $u$  subscript. For example, the most symmetric representation in the  $D_{4h}$  point group to which the molecule  $\text{AuCl}_4^-$  belongs is  $A_{1g}$ . There are four possible letters,  $A$ ,  $B$ ,  $E$  and  $T$ .  $A$  and  $B$  mean that the vibration is singly degenerate.  $E$  means it is doubly degenerate and  $T$  means it is triply degenerate. In the  $C_{2v}$  point group all vibrations are singly degenerate.  $A$  is more symmetric than  $B$ . Across the line from the symbols representing the irreducible representations, there are a series of numbers for each. The numbers are either 1 or -1 and 1 is more symmetric than -1. For example, in the table, an  $A_1$  irreducible representation gives the value of 1 for every symmetry element.



**Figure 3.5.** Two vibrations of water.

Figure 3.5 shows two vibrations of water. By looking at the shape of the molecule it is possible to assign it to the point group  $C_{2v}$  using the methods given above. For the vibration in (a), when the molecule is rotated about the  $C_2$  axis, the direction of the arrow representing a vibration does not change. This is the highest symmetry and is denoted as 1. In addition the direction does not change when the arrow is reflected by either of the planes of symmetry (the plane of the paper and one perpendicular to it which bisects the oxygen). Therefore, the vibration (a) is assigned to the highest symmetry irreducible representation of the  $C_{2v}$  point group ( $A_1$ ). In vibration (b) the sign of the arrow is reversed for  $C_2$  and one plane. When this happens this is given the number  $-1$ . Thus, vibration (b) belongs to a lower symmetry representation. The actual label depends on which plane of symmetry is considered first in the table. It is conventionally given the irreducible representation  $B_1$ .

By this method we can assign a vibration to a particular irreducible representation in a particular point group. For more complex molecules there is a procedure to follow to do this and this is explained in books on the subject [3].

The main advantage of this assignment is that the tables also contain information that enables us to work out whether the vibrations will be allowed by symmetry or not. For infrared, this is done by multiplying the irreducible representation of the vibration by the irreducible representation of  $x$ ,  $y$  or  $z$  which is given in the end column of the point group table in most, but not all, layouts. These correspond to three Cartesian co-ordinates of the molecule and are the irreducible representations of the dipole operator. If this result contains the totally symmetric representation (the highest symmetry representation in a particular point group  $A_1$  in the point group  $C_{2v}$  but  $A_{1g}$  in the point group  $D_{4h}$ ) then the vibration is allowed. The reason this works is that a vibration can be allowed only if the product of the irreducible representations of the ground state, the operator, and the excited state is totally symmetric. Since the ground state is always totally symmetric, it turns out that we only need to multiply the other two. A similar approach is adopted for Raman scattering but in this case we look for the more complex quadratic functions  $x^2$ ,  $y^2$ ,  $z^2$ ,  $xy$ ,  $x^2 - y^2$ , etc., in the table and these are multiplied by the symmetry representation of the vibration. For simple point groups with non-degenerate representations, the rules for multiplying irreducible representations are  $A \times A = A$ ,  $B \times B = A$ ,  $A \times B = B$ ,  $1 \times 1 = 1$ ,  $2 \times 2 = 1$  and  $1 \times 2 = 2$ .

It is unlikely that many readers will carry out an in-depth analysis of this type and in the interests of balance, the reader who requires more information is referred to a group theory book for a fuller explanation [3]. However, the symbols are often used in spectroscopy and the irreducible representations can be used to show if a band is allowed. All readers with serious interests in spectroscopy need to know what they mean.

### 3.8 THE MUTUAL EXCLUSION RULE

One crucial result which arises from this analysis is that irrespective of other symmetry considerations, for a centrosymmetric molecule, only vibrations which are *g* in character can be Raman active and only vibrations which are *u* in character can be infrared active. This is because irrespective of the exact irreducible representation, the *g* and *u* labels can be multiplied out and the final product must contain the totally symmetric representation and hence *g*. The rules are  $g \times g = g$ ,  $u \times u = g$  and  $g \times u = u$ . Since the Raman operators are *g* in character and the ground state is *g*, the excited state must be *g* if the vibration is to be allowed. In contrast, the infrared operator is *u* in character and so the excited state must be *u* if the vibration is to be allowed. Thus, in a molecule with a centre of symmetry, vibrations which are Raman active will not be infrared active, and vibrations which are infrared active will not be Raman active. Note that, as stated in Section 3.2 without proof, it is the symmetric vibrations (*g*) which are Raman active, and the asymmetric vibrations (*u*) which are infrared active. This analysis leads to a rule known as the mutual exclusion rule, which states that any vibration in a molecule containing a centre of symmetry can be either Raman or infrared active, but not both. In molecules without a centre of symmetry, there is no such specific rule. Nonetheless, in general, symmetric vibrations are more intense in Raman scattering and asymmetric vibrations in infrared scattering.

### 3.9 THE KRAMER HEISENBERG DIRAC EXPRESSION

The development of the theory of light scattering is beyond the scope of this book. What we will do here is choose two of the key equations from light scattering theory and develop them to understand in more depth the theory of Raman scattering [4–6]. The intensity of Raman scattering is defined by Equation (3.10):

$$I = Kl\alpha^2\omega^4 \quad (3.10)$$

*K* consists of constants such as the speed of light, *l* is the laser power,  $\omega$  the frequency of the incident radiation and  $\alpha$  the polarizability of the electrons in

the molecule. Thus, two of the parameters which are variable are under the control of the spectroscopist, who can set the laser power and the frequency of the incident light. The way in which  $I$  and  $\omega$  are used to maximize the potential of Raman scattering has already been considered (Chapter 2). The theory is required to understand the role of the molecular property, the polarizability  $\alpha$ .

The equation used to describe polarizability in the molecule is known as the Kramer Heisenberg Dirac (KHD) expression. It is a large equation but it can be easily understood with little in the way of mathematical knowledge. All the terms are defined below and the process being described is the one shown diagrammatically in Figure 1.2:

$$(\alpha_{\rho\sigma})_{GF} = k \sum_I \left( \frac{\langle F|r_\rho|I\rangle\langle I|r_\sigma|G\rangle}{\omega_{GI} - \omega_L - i\Gamma_I} + \frac{\langle I|r_\rho|G\rangle\langle F|r_\sigma|I\rangle}{\omega_{IF} + \omega_L - i\Gamma_I} \right) \quad (3.11)$$

$\alpha$  is the molecular polarizability and  $\rho$  and  $\sigma$  are the incident and scattered polarization directions.  $\Sigma$  is the sum over all vibronic states of the molecule as might be expected from the non-specific nature of scattering. Outside this the remaining terms are constants.  $G$  is the ground vibronic state,  $I$  a vibronic state of an excited electronic state and  $F$  the final vibronic state of the ground state.  $G$  and  $F$  are simply the initial and final states of the Raman scattering process as shown in Figure 1.2. We will consider the numerator and the denominator separately and define the terms in the denominator in due course.

To understand the numerator, consider the numerator in the first term. It consists of two integrals. Because of the complexity of the expression it is usual to write the integrals using 'bra' and 'ket' ( $\langle$  and  $|$ ) nomenclature rather than standard integrals. These integrals are similar to those used in electronic adsorption spectra to describe the absorption and emission processes but since light is not promoted to any actual state of the molecule in Raman scattering, they are better considered as terms which mix the ground and excited states in order to describe the distorted electron configuration in the complex between the molecule and the light. One of the integrals is shown below:

$$\langle I|r_\sigma|G\rangle$$

Starting from the right-hand edge of the expression,  $|G\rangle$  is a wave function to represent the ground vibronic state of the ground electronic state. The operator  $r_\sigma$  is the dipole operator and the mathematical process of it operating on  $|G\rangle$  and multiplying the product with the excited state  $\langle I|$  mixes the two states and when the result is summed over all states. This describes in part the excitation process. A similar process describing in part the scattering process occurs with the left-hand integral to leave the molecule in the final state  $\langle F|$ . Thus, the first of the two triple integrals mixes a ground and an excited state and the second of these integrals mixes the excited state and the final state. Since it is a mixing

between two states which is being described, there is no reason why this process should start in the ground state. Thus, in the second term in Equation (3.11), an equivalent expression to that in the first term is added. This starts with the excited state and mixes the excited and ground states together in the same way. Fortunately, as we shall see when we come to the denominator, this term is less significant in Raman scattering.

Earlier, the nature of the virtual state was discussed and it was pointed out that a virtual state is a real state of the distorted molecule but, since the nuclei do not have time to reach equilibrium, it is not any state of the static molecule. Thus, when the KHD expression is used, the process of distortion is described by mixing all of the vibronic, excited and ground states together to describe electronic states of the molecule which exist only for the instant in which the light is captured. Consider the denominators of terms 1 and 2 in the expression in 3.11. The energy of the term  $i\Gamma_I$  is small compared to the energies  $\omega_{GI}$  and  $\omega_L$ . In term 1, the nearer a specific excited state  $I$  is in energy, to the low energy the smaller the denominator is and the larger part the particular expression for that state will play in the final expression. Further, because  $\omega_{GI}$  and  $\omega_L$  are added in the second expression, the denominator will always be large compared to that in the first term. Consequently term 2 plays a smaller role in describing the polarization process and will now be neglected.

Without  $i\Gamma_I$ , when the frequency of the incident laser light is the same as the frequency of an electronic transition, then the denominator of the first term would go to zero and the result would be that the scattering would become infinite! The term  $i\Gamma_I$  relates to the lifetime of the excited state and affects the natural breadth of Raman lines. Thus, although it is small it is a vitally important part of the basic equation defining molecular polarizability.

Each of the expressions in the numerator of term 1 will depend on the exact nature of the states and the way in which they are coupled through the operator. In this paragraph, we further analyse the KHD expression particularly to understand the selection rules in Raman scattering and to lay the foundation for the resonance Raman approach in Chapter 4. To do this, the states are usually split up into electronic and vibrational components using the Born Openheimer approach. In this approach, the total wave function is split up into separate electronic ( $\theta$ ), vibrational ( $\Phi$ ) and rotational ( $r$ ) components.

$$\Psi = \theta \cdot \Phi \cdot r \quad (3.12)$$

This is a very successful way of approaching many spectroscopy problems. It works because of the difference in the timescale of electronic, vibrational and rotational transitions. The very light electrons involved in a pure electronic transition will change from a ground to an excited state in a timescale in which there is very little movement of the nucleus ( $10^{-13}$  or less of a second). This is the reason electronic transitions are drawn vertically in the conventional diagrams

such as Figure 1.2. The distance along the x-axis which plots internuclear separation cannot alter appreciably during the transition. Vibrational transitions occur in about  $10^{-9}$  of a second and are faster than rotational transitions. Although rotational effects can be seen in gas phase Raman spectra, for the purposes of the limited theory given here, the rotational contribution will be largely neglected.

Thus, because of the different timescales, electronic and vibrational terms can be separated. The term  $\theta$  is the electronic part of the expression and will depend on both the nuclear and electronic co-ordinates ( $R$  and  $r$  respectively) whereas the vibrational term which involves displacement of the heavier nuclei will depend entirely on the nucleic co-ordinates ( $R$ ). The separation between the vibrational and electronic functions allows the integrals in the numerator in the KHD expression to be split up. The electrons travel from one excited electronic state to another so only the electronic term involves the operator.

$$\langle I|r_{\sigma}|G\rangle = \langle \theta_I \cdot \Phi_I | r_{\sigma} | \theta_G \cdot \Phi_G \rangle = \langle \theta_I | r_{\sigma} | \theta_G \rangle \langle \cdot \Phi_I | \Phi_G \rangle \quad (3.13)$$

We can now consider the role of both the electronic and the nuclear part of this equation. The Raman process is so fast that despite the fact that energy is transferred to or away from the nuclei, no appreciable movement can occur during the time of any one scattering event. This means that the electronic part of the wave function can be approximated to what happens when the nuclei are at rest with a correction term to allow for the change in electronic structure when the nuclei move. To make this a little simpler, the electronic integral from the expression above is written as

$$\langle \theta_I | r_{\sigma} | \theta_G \rangle = M_{IG}(R) \quad (3.14)$$

The movement is described by a Taylor series with the value at rest being the first and largest term  $M_{IG}(R_0)$  where  $R_0$  represents the co-ordinates at the equilibrium position. The second and higher terms describe the effect of movement along a particular co-ordinate  $R_{\epsilon}$  and even the second term is relatively small. Thus all but the first and second terms can be neglected. For simplicity the first and second terms are written as  $M$  and  $M'$ :

$$M_{IG}(R) = M_{IG}(R_0) + \left[ \frac{\delta M_{IG}}{\delta R_{\epsilon}} \right]_{R_0} R_{\epsilon} + \text{higher order terms} \quad (3.15)$$

In this way, the KHD expression can be solved. We will not attempt the mathematics here but they can be found in reference 6. Carrying out this procedure leads to the equation below. It looks complex but can easily be simplified.



$$\begin{aligned}
(\alpha_{\rho\sigma})_{GF} = & kM_{IG}^2(RO) \sum_I \frac{\langle \Phi_{R_F} | \Phi_{R_I} \rangle \langle \Phi_{R_I} | \Phi_{R_G} \rangle}{\omega_{GI} - \omega_L - i\Gamma_I} \quad (\text{A-term}) \\
& + kM_{IG}(RO)M'_{IG}(RO) \sum_I \frac{\langle \Phi_{R_F} | R_E | \Phi_{R_I} \rangle \langle \Phi_{R_I} | \Phi_{R_G} \rangle + \langle \Phi_{R_F} | \Phi_{R_I} \rangle \langle \Phi_{R_I} | R_E | \Phi_{R_G} \rangle}{\omega_{GI} - \omega_L - i\Gamma_I} \quad (\text{B-term})
\end{aligned} \tag{3.16}$$

The two terms shown in the equation are known as A-term and B-term. Outside the summation sign, there is a term corresponding either to the electronic component of the Raman scattering ( $M$ ) squared or to  $M$  times the much smaller correction factor  $M'$ . Thus, this part of the expression is much larger in A-term than in B-term. The summation sign ensures a contribution from all excited states to both A-term and B-term. However, as has been stated previously, the closer the excited state is to the laser frequency, the smaller the denominator in the first term of the equation and hence potentially the larger the contribution from the state.

In A-term, the numerator inside the summation sign consists simply of a multiplication of all possible vibrational wave functions. There is a theorem called the closure theorem which demonstrates that when all vibrational wave functions are multiplied together, the final answer is zero. Thus, no Raman scattering will be obtained from A-term. In B-term, an operator, the co-ordinate operator  $R_E$ , is present in the numerator. This operator describes the effect of movement along the molecular axis during the vibration and appears because the correction term  $M'$  has been multiplied out with the vibrational states. One feature of this operator is that the integral will only have a finite value when there is one quantum of energy difference between the initial state on which it operates and the final state. This means that only vibrations containing one quantum of energy will give Raman scattering. Thus, the theory will predict no overtones in Raman scattering and this is a good selection rule. Overtones are not seen unless there is some form of special effect. In addition, it is now possible to see how the Raman selection rule that symmetric vibrations are allowed comes about. The operators in the integrals in the numerator are dipole operators which, as for infrared absorption, are  $u$  in character. However, the Raman process requires that both integrals are multiplied out together. In essence this leads to a final result which is  $g$  in character.

### 3.10 LATTICE MODES

One type of vibrations which has not been considered so far are vibrations created in solid samples by radiation interacting with a lattice. For example, sodium chloride and silicon are materials which give vibrational spectra, but there is no definable molecule in which the atoms are linked by covalent bonds.

In this case, when radiation interacts with the material it induces vibrations through the whole lattice. One type of vibration forms along the direction of propagation of the radiation (longitudinal or L modes) and the other forms at right angles to it (transverse or T modes). These modes form through the whole crystal and each one consists of a very large number of vibrations of similar energy which occupy a band of energies in the material. The band breadth varies depending on the material. By studying bands of this type, as mentioned in Chapter 6, Raman spectroscopy can be used to study the properties of elements such as silicon. These bands are called lattice modes.

In sodium chloride, two types of lattice modes exist. In one type, the displacement is such that the chloride and sodium ions move together and in the other it is such that they move against each other causing a charge separation. The former type of lattice mode is lower in energy, with frequencies falling normally in the acoustic energy range. Modes of this type are called acoustic modes and labelled  $L_A$  and  $T_A$ . The higher energy type are called optic modes and labelled  $L_O$  and  $T_O$ . A full description of these modes is best given through a band theory approach and is outside the scope of this book. However, the term 'lattice mode' and the labels  $L_O$  and  $T_O$  are often used and the reader should be aware of them. In the case of silicon, the effect of loss of order in going from crystalline silicon to amorphous silicon is marked with the Raman spectrum broadening and shifting in frequency. This change is used in the electronics industry (see Chapter 6). In any study in which low frequency modes are important, the possibility of lattice modes being present should be considered.

### 3.11 CONCLUSIONS

The mathematics in Section 3.9 can be quite complex. This is perhaps not surprising since the equations have to describe the molecule in a distorted state at the instant that there is an interaction between the laser radiation and the molecule. However, some of the conclusions are quite simple and the analysis given above provides an insight into the background theory for Raman scattering which helps with problems and more detailed interpretation. Symmetry labels are commonly used in the literature, and at a basic level, the spectroscopist needs to understand their meaning to aid comprehension of many articles. However, the use of symmetry also improves understanding of the nature of vibrations and gives insight into the science that underlies the selection rules. The use of scattering theory is essential to understand the Raman process and such features as the weakness of overtones. It is also essential to understand resonance Raman scattering which forms the subject of Chapter 4. However, much of the rest of this book after Chapter 4 can be understood with only a minimum appreciation of the contents of this chapter.

## REFERENCES

1. D. Long, *The Raman Effect: A Unified Treatment of the Theory of Raman Scattering by Molecules*, John Wiley & Sons, 1977.
2. J.R. Ferraro and K. Nakamoto, *Introductory Raman Spectroscopy*, Academic Press, San Diego 1994.
3. F.A. Cotton, *Chemical Applications of Group Theory*, Wiley Interscience, 1990.
4. R.J.H. Clark and T.J. Dines, *Angew. Chem., Int. Ed. Engl.*, **25**, 131 (1986).
5. R.J.H. Clark and T.J. Dines, *Mol. Phys.*, **45**, 1153 (1982).
6. D.L. Rousseau, J.M. Friedman and P.F. Williams, *Topics in Current Physics*, **2**, 203 (1979).

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# Chapter 4

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## Resonance Raman Scattering

### 4.1 INTRODUCTION

In the early days of Raman scattering, many spectroscopists preferred to avoid coloured compounds. After all, if a powerful beam of visible radiation is used to excite a molecule which is coloured, the light is liable to adsorb into the sample. This can cause strong fluorescence and prevent Raman detection. Even if it does not, it can cause sample decomposition through photodecomposition or heating. However, when the frequency of the laser beam is close to the frequency of an electronic transition, scattering enhancements of up to  $10^6$  have been observed and they are quite often of the order of  $10^3$  or  $10^4$ . This means that Raman spectroscopy becomes a much more sensitive technique and since only the chromophore gives the more efficient scattering, it will also be selective for the part of the molecule involving the chromophore. When the resonance condition occurs, it turns out that it is possible to get electronic as well as vibrational information from the sample. One key reason this technique has become important is that the molecules give rise to good Raman scattering rather than intense fluorescence. They include the porphyrin rings which are present at the centre of a number of key enzymes, the pigments made from phthalocyanines, and other important classes of molecules such as the polyacetylenes. For these species, resonance Raman scattering can give extremely informative *in situ* analysis and for this reason the use of resonance has been growing in recent years. The theory is well described in a number of reviews (see references [4–6] of Chapter 3). Here we will not carry out a rigorous mathematical treatment but concentrate on understanding the mechanism which underlie the equations used.

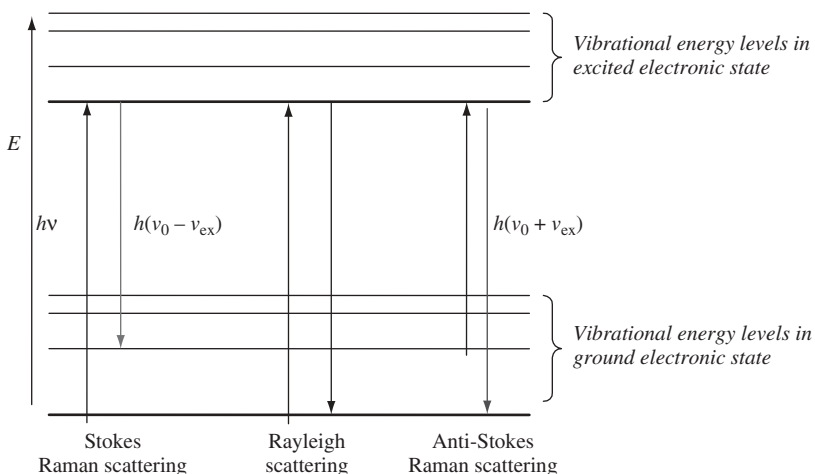
## 4.2 THEORETICAL ASPECTS

### 4.2.1 The Basic Process

To obtain resonance Raman scattering, a laser beam is chosen which has an excitation frequency close to that of an electronic transition. Ideally, a tuneable laser would be used for excitation and the frequency would be chosen to correspond exactly to the energy difference between the ground vibrational state and the first or second vibronic state of the excited state. This condition is shown in Figure 4.1. Fortunately, the maximum resonance Raman scattering is not required for observing the effect or to obtain some enhancement. It is often more practicable to use an existing laser line available in the laboratory which has a frequency as near as possible to the true resonance frequency.

Figure 4.1 could also be used to explain the nature of the absorption process in electronic absorption spectroscopy. It shows a transition from the ground state to an excited state. The key difference, which cannot be seen in the diagram, is the length of time the molecule remains in an excited state. As we know from Chapter 3, the scattering process is fast, with scattering (the downward process in the diagram) occurring before the nuclei reach equilibrium positions in the excited state. In contrast, in absorption, the upward transition is also fast but the electron is absorbed into the molecule and the nuclei relax to the equilibrium geometry of the excited state. Thus, the processes of resonance Raman scattering and absorption are separated clearly by time, a variable not shown in the diagram.

Further, in the practice of absorption spectroscopy, the light irradiating the sample is usually polychromatic covering a wide range of frequencies, and



**Figure 4.1.** Diagram of the basic process of resonance Raman scattering.

under these circumstances a number of transitions are involved. Often, the most intense transition is to one of the higher vibronic levels. The rounded shape of absorption bands is partly due to contributions from a number of levels and partly to the presence of hot bands arising from electrons present in excited states. However, as we shall discuss later in this chapter, the theory predicts that the most intense resonance Raman scattering in some cases will come mainly from the first two vibronic levels. As a result, it is not necessarily the case that the maximum absorbance of a UV visible transition is the energy at which the greatest resonance Raman scattering will be obtained from the excited state.

Clearly, with radiation of a frequency suitable to cause resonance, absorption as well as scattering will occur. When absorption occurs, the energy may be lost either by transfer to the lattice and dissipation as heat or as fluorescence. The ratio of scattering to absorption is a property of the molecule and is difficult to predict. From a practical point of view, fluorescence interference limits the number of molecules which will be suitable for examination by resonance Raman scattering.

The increase in intensity from resonance enhancement can be understood by studying the KHD equation analysed in Chapter 3 (Equation (3.11)). Here we will explain how the effect occurs with minimum reference to the mathematics. Full accounts of the mathematics and more in-depth references can be found in the references to Chapter 3. Consider the denominator of the first term. The resonance condition is met when the energy difference between the lowest vibrational state of the ground electronic state  $G$  and the resonant vibronic state  $I$  ( $\omega_{GI}$  in Equation (3.11)) is of the same energy as the exciting light  $\omega_L$ . This would mean that the denominator of the first term reduces to  $i\Gamma_I$ , which is a small correction factor. In some early forms of this equation it was not present, but it is required to take account of the lifetime of the excited state. Thus, under resonant conditions the denominator is very small and this will lead to the first term becoming very large, increasing polarizability and giving very much greater Raman scattering. Fortunately, in the second term in Equation (3.11),  $\omega_{IF}$  and  $\omega_L$  are additive and consequently this term can be neglected.

Another key difference between resonance Raman scattering and Raman scattering is immediately obvious from the KHD equation. In the resonance condition, almost all the interaction is with the one state, so that the  $\Sigma$  sign in the KHD equation can be dropped. This means that the scattering will depend on the properties of that state. As a result, the closure theorem, which states that the sum of all the vibrational matrix elements of a molecule is zero, is no longer valid. This was the reason that the A-term in Equation (3.16) did not predict any Raman scattering and since it is no longer valid, the A-term as well as the B-term can give resonance Raman scattering. This leads to two forms of resonance Raman scattering which have quite different properties.

For B-term scattering, as described in Chapter 3 (Equation (3.16)), the co-ordinate operator  $R_g$  allows a transition only if there is one vibrational unit difference between the ground and the excited states. That is, no overtones were

predicted. However, in A-term scattering there is no co-ordinate operator in the numerator. As a result, overtones in resonance Raman scattering, where it arises from A-term, will be allowed and there is no reason why they should not be intense. We shall see later some examples where there are intense overtones from A-term resonance Raman scattering. Further, in B-term scattering although the co-ordinate operator still exists, it is no longer a sum over a large number of states. As a result of this and possibly because of higher terms which result from a more complete analysis of the KHD equation, the overtone selection rule is not as effective in B-term resonance Raman scattering as in Raman scattering, and weaker overtones are obtained.

The interaction of the exciting radiation with the excited electronic states of the molecule is different in A-term and B-term enhancement. In A-term, the excitation which causes the scattering simply couples the ground state and the excited state as described previously. This type of scattering is called A-term or Franck Condon scattering. The electronic term  $M$  is much larger for scattering which arises from an A-term mechanism than from a B-term mechanism since it is  $M^2$  as opposed to  $M \times M'$  and A-term scattering might be expected to give more intense spectra than B-term (see Equation (3.16)). However this is only one factor. To obtain intense scattering, the transition should start from a point where there is considerable electron density in the ground state and go to a state where the wave function is such that, once populated, there will also be considerable electron density. Since the transition is vertical, this is often called good overlap between the states. In addition the selection rules must not prohibit the transition. This is similar to the conditions required for an intense allowed electronic transition in electronic spectroscopy. The matrix elements for the two processes are the same, which is not surprising, but it suggests that resonance enhancements will be most intense with allowed electronic transitions. In addition, strong A-term resonance enhancement occurs when there is a difference in the nuclear geometry between the ground and excited states.

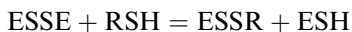
In the B-term case, two excited states are mixed through the co-ordinate operator  $R_e$ . Every time the molecule moves, and the geometry changes, there will be a need to remix the electronic states to obtain states new to the molecule. Thus, if there are two  $\pi \rightarrow \pi^*$  transitions reasonably close together in the visible region, as is the case with porphyrins and phthalocyanines, then the co-ordinate operator will help to mix these two together. This type of more complex enhancement is called B-term or Herzberg Teller enhancement. One of the differences between A- and B-term enhancement is that B-term enhancement is only strong from the zero and first vibronic states of the excited state in resonance. There is no restriction on the excited vibronic states which can give A-term enhancement. In addition, B-term enhancement can arise from weak or forbidden transitions. For example the lower energy  $\pi \rightarrow \pi^*$  transition of porphyrins is forbidden and weak, but B-term scattering from this transition is appreciable. This is because the orbital mixing process involves the higher energy  $\pi \rightarrow \pi^*$  transition which is allowed.

#### 4.2.2 Electronic Information

In Raman scattering, the KHD expression sums a number of small terms over all vibronic excited states of the molecule. As a result, it is difficult to obtain any electronic information from the spectrum. However, in resonance Raman scattering, one particular vibronic excited state is picked out as providing much of the enhanced scattering. As a result, the nature of the scattering depends on the nature of that state. It should be noted that other vibronic states close in energy to the one in resonance may also contribute, but it is easier to explain the effect by concentrating on one single state.

With A-term scattering, as stated above, no resonance enhancement will be obtained unless there is a change in the nuclear distances between the ground and the excited states. This actually means that small molecules such as iodine provide good A-term enhancement. In some of the older reviews it is stated that small molecules are the only molecules that give A-term enhancement. This is not completely true. Although large nuclear displacements between any two atoms are not usually obtained with large molecules, the sum of the many small displacements that occur can still give an appreciable nuclear displacement and therefore A-term enhancement.

To understand the effect that nuclear displacement has, it is necessary to consider the timescales of electronic and vibrational movement again. In essence, vibrational movement occurs over a longer timescale than Raman scattering. As a result, during the complete excitation and scattering process caused by any one photon, the molecule can be at any place along a vibrational co-ordinate. Since effective overlap between the ground state and the excited state in resonance is required to achieve the most efficient Raman scattering, it is necessary that this overlap is present through at least most of the vibrational cycle. A good example of this is in the resonance Raman spectrum of the molecule 5,5'-dithiobis-2-nitrobenzoic acid, and an ion which arises from it. This is a standard reagent used in electronic absorption spectroscopy to measure thiols in molecules since it provides coloured ions on reaction with thiols. The reactions are shown below. The compound, which was first used by Ellman, is often called Ellman's reagent, and here is simplified to ESSE.



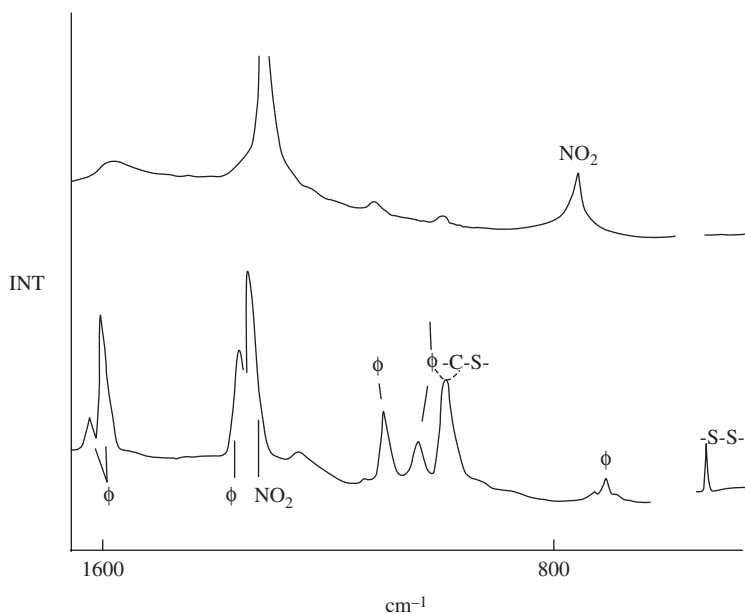
pH 7.4



The original molecule ESSE has an absorption band at 325 nm. However, the coloured ion  $\text{ES}^-$  formed at neutral pH has an absorption band at 410 nm. When a laser with an excitation wavelength of 457.9 nm (this was the closest wavelength to 410 nm available in the laboratory at the time) was used to excite ESSE,



a typical Raman scattering spectrum was obtained with bands arising from vibrations of the phenyl rings ( $\phi$ ), the nitro group and the S-S bond identifiable. This gives an example of normal or perhaps pre-resonant spectra with most vibrations that would be expected to occur in the spectral region studied being present in the spectrum. However, the Raman scattering from  $\text{ES}^-$  is much nearer to resonance and consequently much stronger. The spectrum of ESSE (Figure 4.2) was obtained from a  $10^{-2}$  M solution, but to obtain an approximately equal intensity of scattering, the spectrum of  $\text{ES}^-$  was obtained from a  $10^{-5}$  M solution. Because  $\text{ES}^-$  is near to resonance, the bands which are resonantly enhanced depend on the excited state in resonance. The spectrum consists of only two main peaks which are assigned to the nitro group stretch and bend. On the assumption that this is A-term scattering, to get effective resonance enhancement a nuclear displacement and good overlap are required. The biggest change in nuclear displacement of this molecule will be along the nitro group bonds. The high intensity of the stretching motion along these bonds suggests that the excited state has an electronic geometry which is elongated along the bond thus giving good overlap at any point on the main stretching vibration. This experiment indicates the selectivity of resonance Raman scattering and also one of the ways in which electronic information can be obtained.



**Figure 4.2.** The spectrum of Ellman's reagent at  $10^{-2}$  M and of the anion  $\text{ES}^-$  at  $10^{-5}$  M.

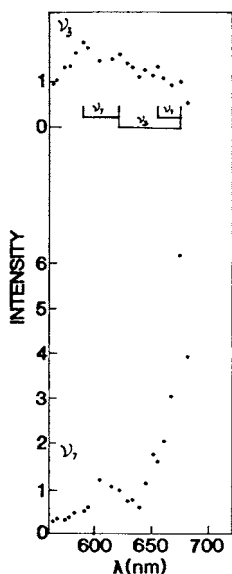
Another clear difference between normal Raman scattering and resonance Raman scattering is that in both cases the intensity is dependent on the fourth power of the frequency, but in resonance Raman scattering the intensity is also strongly dependent on how close the frequency of the excitation used is to that of the frequency of an allowed electronic transition. It is worthwhile to look at the KHD expression once again. As previously discussed, in the resonance condition the denominator is very small. However, as the difference between the laser excitation frequency and the transition frequency increases, the resonance enhancement will drop off quite quickly. If the total intensity obtained in resonance is given the value 1, then 10 wavenumbers away from resonance the enhancement will be down to about a tenth and at a 100 wavenumbers about a hundredth, etc. Thus, we need to be quite close to resonance to get the maximum enhancement. Perhaps of more importance and not widely recognized by many Raman spectroscopists is what happens far away from resonance. Supposing for example the total enhancement obtained was  $10^4$ , then 10,000 wavenumbers away from resonance, an enhancement of one would be obtained. Thus, there is a very long tail on the frequency dependence of the resonance enhancement process and it could be that even with infrared excitation, enhancement factors of 5 or greater could be obtained for molecules with visible chromophores. This may seem trivial compared to the enhancements that can be obtained close to resonance but it does mean that a coloured part of a molecule could easily have a spectrum five times as intense as would have been expected in an ordinary Raman spectrum even if an FT infrared system is used. If the molecule is a strong Raman scatterer this can mean that a minor component can be picked out selectively. We will show later in this book (Chapter 6) that this can be used to good effect, for example in looking at ink jet dyes with Raman scattering obtained with an infrared laser.

The above explanation is over simplified. It should be noted that for any one process a number of vibronic bands which are near but not quite in resonance would contribute and this will change the frequency/intensity relationship. The greater the separation between the laser frequency and the frequency of the resonant excited state, the more appreciable the contributions from other vibronic states is to be expected until normal Raman scattering is essentially restored.

#### 4.2.3 Resonance Excitation Profiles

Since the absolute and relative intensities of the bands in a resonant spectrum are dependent on the separation between the excitation and resonance frequencies and on the nature of the electronic states, it can be useful to plot the intensity of selected bands against the frequency of the laser. This is called a resonance excitation profile (REP) and to do this effectively, a tuneable laser is

preferred so that the Raman spectrum can be recorded at a large number of different laser frequencies. An approximation to this can sometimes be achieved by using a multiline laser if the absorption band is sufficiently broad and there are enough lines from the laser available in the energy region covered by the absorption band. In the simplest REP, the maximum intensity of the band produced will be the point at which resonance occurs. If the vibration plotted is resonant with more than one vibronic level, more than one peak should be seen in the profile. Also, since this is resonance and not all vibrations are affected in the same way, the profiles will vary from one vibration to another. This information can be difficult to obtain and requires quite sophisticated equipment. However, it provides unique and extremely valuable information to probe in depth the electronic and vibrational structure of a particular molecule. An example of a resonant excitation profile for two different vibrations is shown for the phthalocyanine molecule in Figure 4.3. One,  $\nu_3$ , is at a relatively high frequency and the structure on the profile indicates that a number of vibronic states are involved. This is reinforced by the upward slope to higher frequencies and suggests some A-term enhancement. The lower frequency vibration,  $\nu_7$ , shows two main bands more typical of B-term enhancement. A weaker peak can also be seen on the low energy side of the main band in the  $\nu_7$  profile. This is because the excited state of the phthalocyanine is split



**Figure 4.3.** Resonant excitation profiles for two copper phthalocyanine vibrations —  $\nu_3$  and  $\nu_7$  created using different excitation wavelengths.

by a dynamic Jahn Teller effect and the extra weak band arises from a profile due to a second electronic state.

The above description provides only a qualitative understanding of the nature of resonance Raman scattering. A more in-depth review can be obtained in the references to Chapter 3. However, enough has been said to make practical use of resonance Raman scattering and also to interpret the basic effects seen in the spectra. Table 4.1 gives the main similarities and differences between Raman scattering and resonance Raman scattering.

**Table 4.1.** Main differences between Raman scattering and resonance Raman scattering

Raman scattering	Resonance Raman scattering
B-term effective	A- and B-term effective
No overtones	Overtones common
More modes observed in the spectrum	Some modes selectively enhanced
No electronic information	Electronic information present
Weak scattering	Stronger scattering

### 4.3 PRACTICAL ASPECTS

As already discussed, in resonance Raman scattering the laser energy is chosen to match as closely as possible that of an absorption band of the analyte. As a result, absorption will occur which may cause both sample decomposition and fluorescence depending on the nature of the material. Therefore, the spectroscopist must develop a strategy which minimizes these effects. To assess the extent of the problem, one obvious thing to do is to observe the sample before and after exposure to the laser beam. Very often with resonance Raman scattering, sample damage can be clearly seen in a coloured sample as a change in colour or a black spot. However, in some cases, such as with proteins containing the heme group, lower powered radiation alters the protein structure but does not destroy the heme and hence there is little to no visible change in colour. It is important that the spectroscopist recognizes these subtle changes. In principle, it would be easy to check this using absorption spectroscopy. However, the difference in sample volume actually interrogated in Raman scattering and in absorption spectroscopy can give misleading answers. In most absorption spectrometers, the sample is placed in a 1 cm cuvette and the beam passes through a significant part of the sample volume whereas if Raman scattering is obtained from the same cuvette, it is usually obtained from a small focussed volume. Damage, which occurs in this volume in a short time, will affect the Raman scattering, but may not be sufficient to be observable in the absorption spectrum of the bulk of the sample.

One way to minimize photodegradation is to use a sampling method in which the sample passes through the laser beam but does not stay in the beam for the whole time of the analysis. This way any one part of the sample is not retained in the beam for any lengthy period of time. Raman scattering is then obtained from the cumulated spectra from a large area of the sample. For example, with solid samples, spinning disks are often used, as already mentioned in Chapter 2, Section 5. In this technique, the sample is pressed into a disk, or compressed into a channel cut in a blackened support disk. The laser is then set to focus on the outer part of the disk or onto the channel in the disk and the disk spun. In this way, scattering is collected from the point at which the beam is focussed but the sample precesses through the beam limiting the exposure time of any one area of the sample. This process allows excited states to relax and heat to diffuse away from the sample before the disk completes a revolution and the same part of the sample is interrogated again. This is effective, although in many samples, the track where the sample has decomposed can clearly be seen. It still means there is less decomposition than would be present in a statically focussed sample.

Similar devices can be devised for use with solution samples (Chapter 2, Section 5). They usually consist either of a spinning sample holder, such as an NMR tube with the beam tightly focussed close to the surface, or a small flowcell where the sample can either flow through or oscillate back and forward under the laser beam.

The spectroscopist has another approach which may be effective. As discussed earlier in this chapter, the resonance contribution extends over a range of frequencies decreasing as the difference between the frequency of the absorption band and the excitation laser increases. Thus, by moving the frequency of excitation away from the resonance frequency to a pre-resonance frequency, it is possible to avoid the worst effects caused by absorption of the excitation while still retaining a degree of enhancement. With pre-resonance excitation as discussed above, it should be borne in mind that the further away from resonance the spectrum is recorded, the more normal Raman scattering selection rules will apply. In addition, with molecules of high symmetry, the different symmetry types of vibration have different dependencies of resonance enhancement on frequency.

This type of experiment highlights another possible problem with resonance. In a non-resonant sample, a visible laser beam can be focussed tightly within the media and although there are refraction and reflection effects, they are minor compared to those obtained on focussing into a coloured solution to obtain resonance. In normal Raman scattering, the focussed spot created by the laser beam can be effectively imaged back onto the detector. However, in the resonant condition, the laser light is absorbed by the medium and the deeper it penetrates, the less intense is the light. Thus, the focussed spot may occur at a position in the sample where there is relatively little laser power. Further, the

scattered radiation is much weaker than the exciting radiation and is given out as a cone. Therefore, it will be absorbed rapidly as it passes back through the sample. This effect is called 'self-absorption' and can make resonance Raman scattering difficult to obtain despite the enhancement.

In solution, there is usually a concentration range in which resonance scattering is effective. If the sample is too concentrated, the beam may be so attenuated as to be weak at the focus spot and in this condition, self-absorption of the scattered radiation will prevent effective collection of the Raman scattering. In addition, where there is beam penetration into the sample, local heating caused by absorption can cause a change in the dielectric constant of the medium, and cause a lensing effect along the beam. This makes it much more difficult to collect the light effectively. However, if the sample is too dilute, the Raman scattering will be too weak to detect. Thus, it is important while measuring solution resonance Raman scattering to recognise that if poor scattering is obtained, it may be necessary to dilute the sample rather than increase the concentration. It is possible to find the right concentration only by trial and error.

To minimize these effects, the beam should be focussed close to the sample surface, but there is a limit as to how well this can be done. In a solid, specular reflection from the surface can occur if the beam is focussed directly on the surface, and in solution, focussing too close to the glass wall at the front of the sample can cause intense reflection from the glass. The sudden appearance of more intense light under these conditions usually means that the laser is focussed on the glass rather than on the solution. This apparently intense scattering can mislead the spectroscopist into recording spectra of the wall of the vessel rather than the solution. The ready availability of disposable plastic cuvettes has made this a more serious problem. When focussing through them, the spectrum of the plastic is not usually observed, but if the beam is focussed on the wall of the cuvette, excellent spectra can be recorded from the polymer material which can easily be mistaken for the spectrum from the sample.

Despite these problems some key results can be obtained from resonance Raman scattering which make it an important technique in some fields. Some examples of where it is effective are given in Section 4.4.

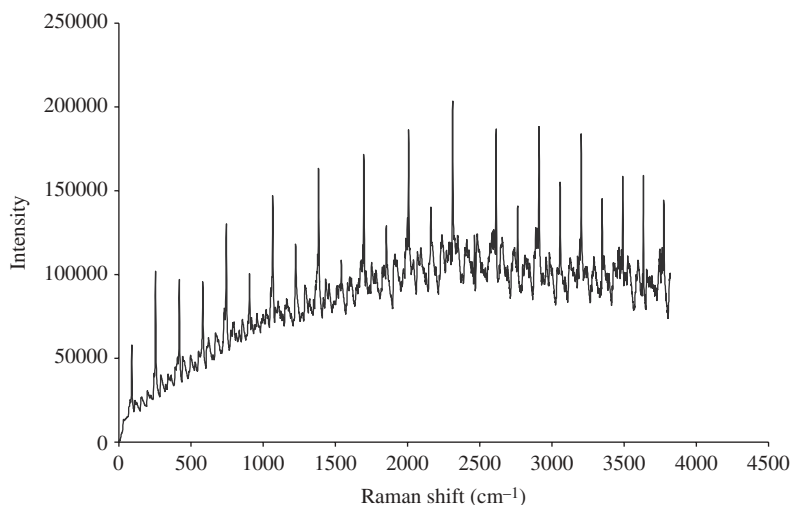
## **4.4 EXAMPLES OF THE USE OF RESONANCE RAMAN SCATTERING**

### **4.4.1 Small Molecules**

The Raman spectra of iodine is a classic example of A-term resonance enhancement from a small molecule. Excitation of  $I_2$  vapour obtained by heating some iodine in a vapour cell produces a remarkable spectrum consisting of a series of

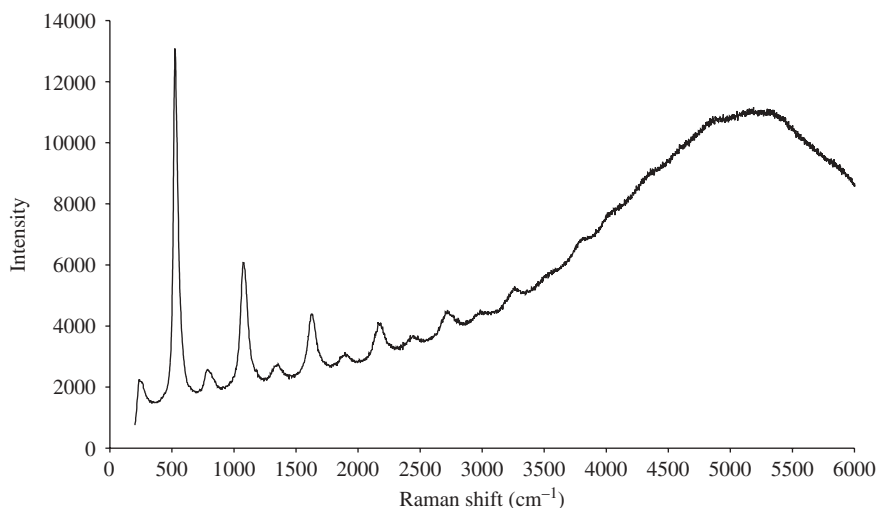
sharp lines which are very intense (see reference 6 of Chapter 3). As discussed in Chapters 1 and 3, we expect one vibration from a diatomic molecule in the gas phase and the frequency of the lowest energy peak corresponds approximately to the energy we would expect from Hooke's law. The other peaks appear at regular intervals and the energy between them is approximately one quantum of the same energy as that of the vibration. A similar experiment is easily performed either by using a solution of iodine or by focussing onto iodine as a solid. Figure 4.4 shows the spectrum of solid iodine recorded from an iodine crystal using a Raman microscope and 514.5 nm excitation. Again there is a regular pattern of bands but the bands here are broader due to solid state effects.

We are able to learn more about the nature of iodine from this spectrum than we would from conventional Raman scattering. First, the nearly equally spaced bands are due to the fundamental and overtones of the one vibration. The fundamental is the lowest energy peak and some overtones are more intense than the fundamental! This is clearly A-term scattering in which there is no selection rule to forbid the overtones occurring. Secondly, with the harmonic approach, we would expect the overtones to be equally separated in energy. However, as discussed in Chapter 3, with the true Morse curve, the separation decreases towards higher energies as a result of the non-harmonic nature of the curve. Thus, by studying the changes in separation, it is possible to calculate the shape of the Morse curve. This is another example of Raman scattering providing electronic information.



**Figure 4.4.** The resonance Raman spectrum for solid iodine taken with 514.5 nm excitation.

A second example of A-term scattering is given in Figure 4.5 for the pigment lapis lazuli. A synthetic form of this is widely used as the pigment ultramarine. For many years, the colour in this compound was a mystery. However, it is now known to be due to the small sulphur species,  $S_3^-$  and  $S_2^-$ , which are trapped in an oxide lattice. It is the transitions from these ions and particularly  $S_3^-$ , which give the colour in the visible region. Figure 4.5 shows the resonance Raman scattering taken from a sample of ultramarine using 406 nm radiation for excitation. This wavelength will enhance the intensity of  $S_3^-$  over  $S_2^-$  since it is closer to resonance with it.  $S_3^-$  will have more than one possible vibration, which could be observed in the Raman scattering. In essence, a symmetric stretch and a bend are the most likely to appear. The band at about  $500\text{ cm}^{-1}$  is the fundamental mode of the stretch. The fundamental of the bend is closer to the exciting line and not observed because of the filter used. The bands at higher energy are overtones and combination modes of the two fundamentals. The most intense fundamental band is the stretch and the most intense peaks with regular separations are the overtones of it. Again, there is a slight decrease in the frequency of the separations between the bands for higher overtones and this information can be used to calculate the nature of the Morse curve for the ground state of ultramarine. The weak band just above the fundamental of the stretch is a combination mode corresponding to one quantum of the stretch and one of the bend. Further, by using a different frequency (normally 457.9 nm radiation from an argon ion laser) it is possible to ensure a greater enhancement of the peaks due to  $S_2^-$  and consequently to estimate *in situ* the approximate ratio of  $S_2^-$  to  $S_3^-$  from resonance Raman scattering.



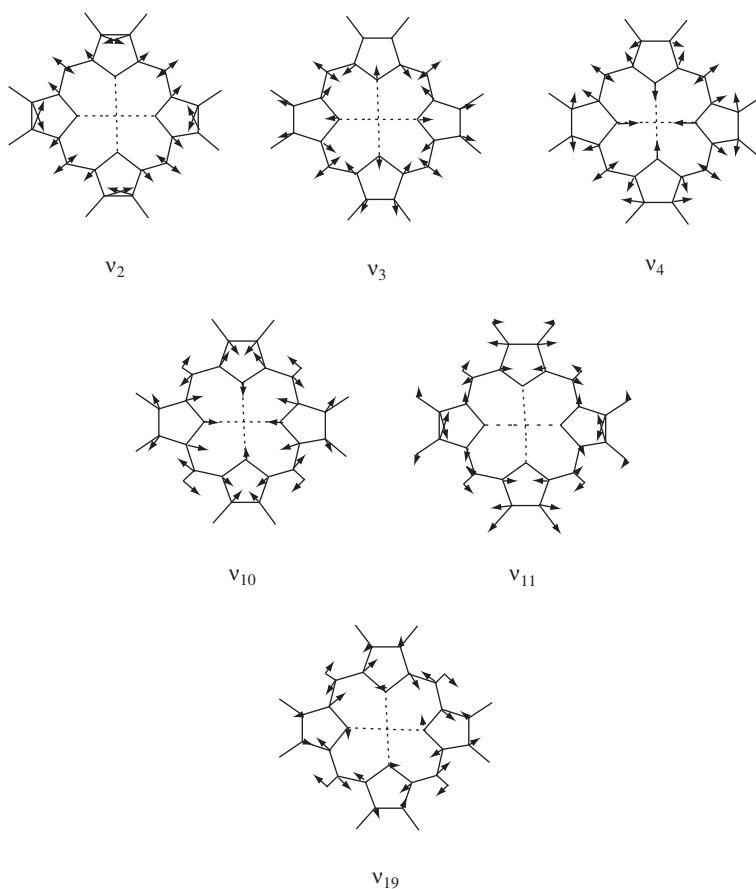
**Figure 4.5.** The resonance Raman scattering taken from a sample of ultramarine using 406 nm excitation. The broad underlying band is fluorescence.



#### 4.4.2 Larger Molecules

Perhaps the most widespread use of resonance Raman scattering is for the study of heme-containing proteins and there are good reviews on this topic [1, 2]. The resonance Raman scattering obtained with visible radiation from these proteins is due to an interaction with the  $\pi \rightarrow \pi^*$  transitions from the porphyrin ring of the heme group (Figure 4.6).

Detailed assignments of the vibrations have been made and some of these vibrations which appear strongly in resonance Raman scattering can be linked to structural properties. For example, the top three vibrations shown in Figure 4.6 are used as markers for the oxidation state and spin state of the ion. The

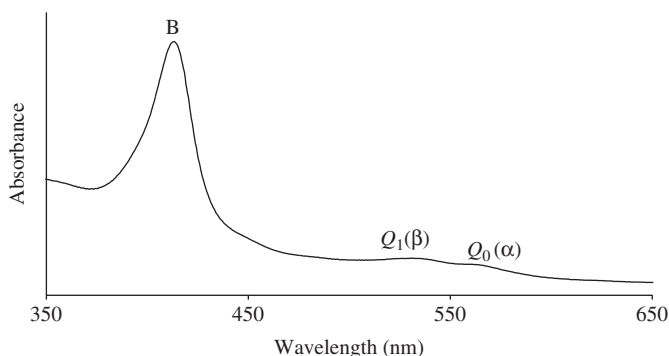


**Figure 4.6.** Typical vibrations taken from a porphyrin ring system (the symbol printed below each of the diagrams are the conventional ones used to describe that particular vibration).

oxidation state marker,  $\nu_4$ , shifts more in frequency than other bands when the oxidation state of the iron ion in the centre of the ring is changed. The reason for this can easily be seen. One of the largest displacements is on the four nitrogens attached to the central metal ion. They move symmetrically inwards and outwards in phase to alter the size of the hole in the centre. Thus, the size of the metal ion which fills this hole and which changes as the oxidation state changes would be expected to have a significant effect on the frequency of this vibration. The reason why  $\nu_3$  and  $\nu_{10}$  act as spin state markers of the iron is more subtle. Their common feature is that they have significant displacements on the inner ring system of the porphyrin. There is much more information to be obtained from these spectra. For example, in protoporphyrin IX there are two vinyl groups attached to the porphyrin ring system which are quite often not in the plane of the porphyrin ring. When this is the case there is only very weak conjugation between the vinyl groups and the heme system, and hence the intensity of the vinyl groups is low since there is little resonance enhancement. However, when they become planar with the ring, the conjugation increases and the band intensities increase. Thus, bands assigned to the vinyl groups can be important in deciding the position of these groups relative to the heme system. This alters with some protein-functional changes. Other vibrations which give effective Raman scattering can be related to the amount of doming or ruffling on the porphyrin ring.

The heme group has two sets of electronic absorption bands in the visible region as shown in Figure 4.7. The most intense band is the Soret band at about 410–450 nm and there are weaker bands between 500 and 650 nm called the  $\alpha$ 1 and  $\beta$  or  $Q_0$  and  $Q_1$  bands.

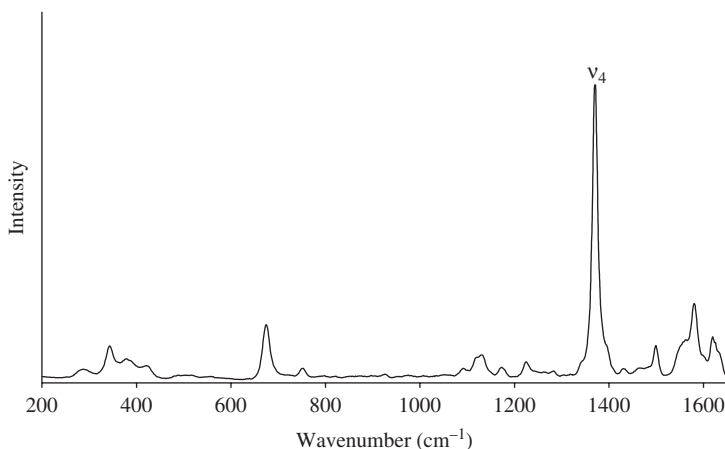
Excitation at the frequency of the Soret absorption band produces Raman scattering in which the  $A_{1g}$  vibrations are prominent. This might be expected, since if the heme ring is regarded as flat and peripheral groups such as the vinyl groups are ignored, it belongs to the  $D_{4h}$  point group. Thus, with an intense



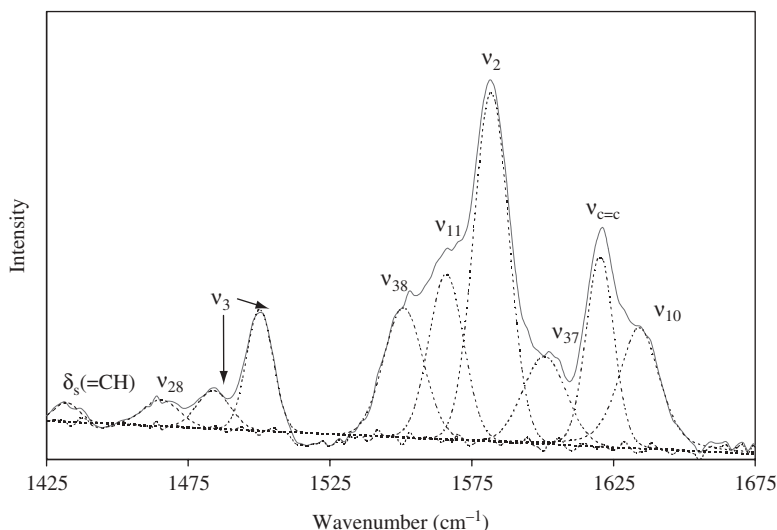
**Figure 4.7.** Absorption spectra for a typical porphyrin system.

allowed band such as the Soret band we would expect A-term scattering and hence the totally symmetric modes should be enhanced. However, other bands that appear in the spectra suggest there is also some B-term scattering.

When in resonance with the  $\alpha_1$  and  $\alpha_2$  bands, it is the  $B_{1g}$  and  $B_{2g}$  modes which tend to be the most enhanced, although  $A_{1g}$  modes can often be observed. We would expect this change of emphasis. B-term enhancement uses the Hertzberg Teller mechanism which was discussed very briefly at the end of 4.2.1 for this case. The co-ordinate operator mixes two excited states. Here the forbidden  $\pi \rightarrow \pi^*$  transition which gives rise to the weak  $\alpha_1$  and  $\beta$  absorption bands is in resonance with the laser. The states mixed are those which give rise to these bands and the Soret band. Effective mixing of the states requires a less symmetric vibration and hence the enhancement of the  $B_{1g}$  and  $B_{2g}$  bands. Figure 4.8 shows the resonance Raman scattering taken with 406 nm excitation from a P450 protein. It is expected in this spectrum that the most symmetric bands will dominate but the other bands will also be present. The most intense band is  $\nu_4$ , the oxidation state marker, at  $1372\text{ cm}^{-1}$ . This energy position is characteristic of iron in oxidation state III. The bands  $\nu_{10}$  and  $\nu_3$  are weaker but they are at energy positions which clearly indicate that this protein is in the high spin form. A more in-depth analysis of the complex spectra obtained in the  $1600\text{--}1550\text{ cm}^{-1}$  region makes it clear that there are other changes occurring. These refer to the vinyl groups and the ring doming/ruffling described earlier. To analyse the spectrum which is shown in Figure 4.9, curve fitting procedures were used. The dangers of this approach were discussed in Chapter 2. In this



**Figure 4.8.** The resonance Raman scattering from a P450 protein taken with 406 nm excitation.

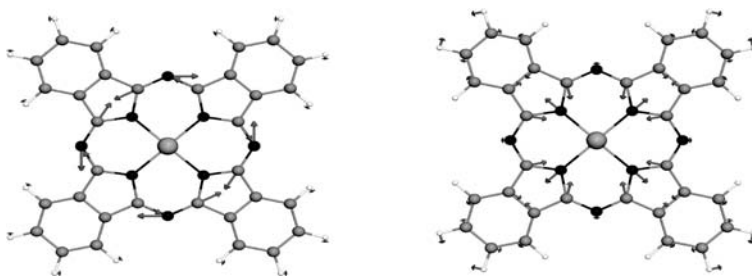


**Figure 4.9.** Spectra in the region from 1500 to 1650  $\text{cm}^{-1}$  taken with 406 nm excitation and curve fitted. (Reproduced with permission from W.E. Smith and S.J. Smith, *Biopolymers*, **70**, 620–627 (2003).)

case, there is a wealth of related literature which makes some but not all the assignments definite but data of this type is best used with other evidence.

P450 proteins are large with a complex structure. Despite the very large number of atoms and bonds in this molecule the resonance spectrum picks out clearly the bands due to the heme to give a very good selective spectrum. However, it raises an interesting question as to what has happened to the normal Raman scattering from the rest of the protein. After all, given the large number of atoms which will contribute to non-resonant but Raman active vibrations, it would be expected that the summation of all vibrations of a particular molecule might appear as a broadened band somewhere in the spectrum. In fact, normal Raman scattering from a protein is weak but can be obtained. In the presence of strong resonance Raman scattering it is seldom seen.

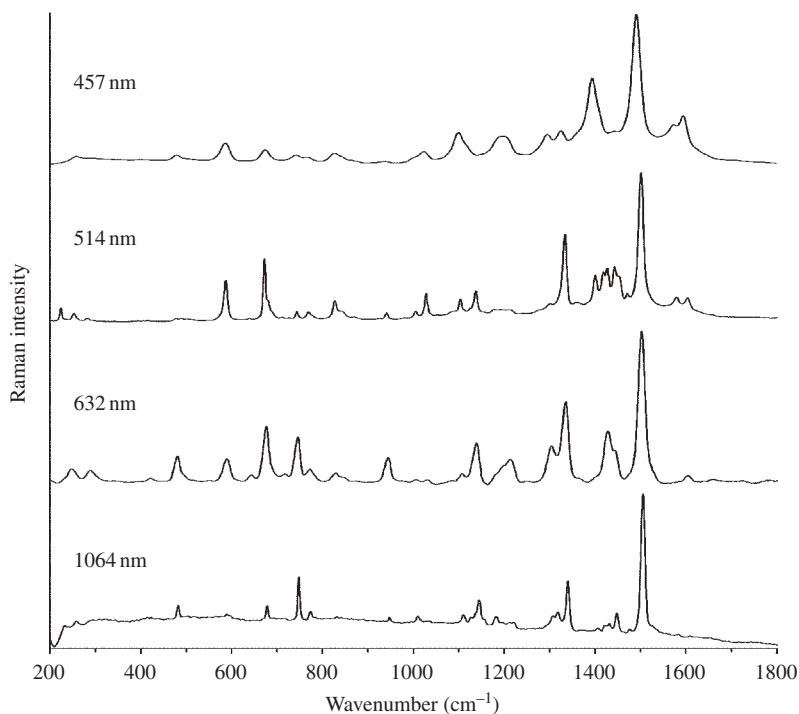
This raises a general question about Raman scattering. Some types of vibration such as the vibrations of water are very weak and other vibrations even with normal Raman scattering can be quite strong. Thus, Raman scattering has a natural selectivity which here has been enhanced by using bands which would normally be quite strong in normal Raman scattering, under resonant conditions. The Raman spectroscopist really needs to consider this when considering the use of Raman scattering for a particular problem. If the species to be detected gives strong Raman scattering, either because the normal Raman scattering is strong, or because it is in resonance, it may well be a very effective technique. However, if the Raman scattering from the matrix is strong and



**Figure 4.10.** Two characteristic vibrations of copper phthalocyanines.

from the substance which it is desired to detect it is weak, it may be difficult to obtain an effective spectrum.

Many other important molecules give resonance Raman scattering. One widely used class of pigments which give excellent resonance Raman scattering are the phthalocyanines. In Figure 4.10, two of the many vibrations in the molecule are shown.

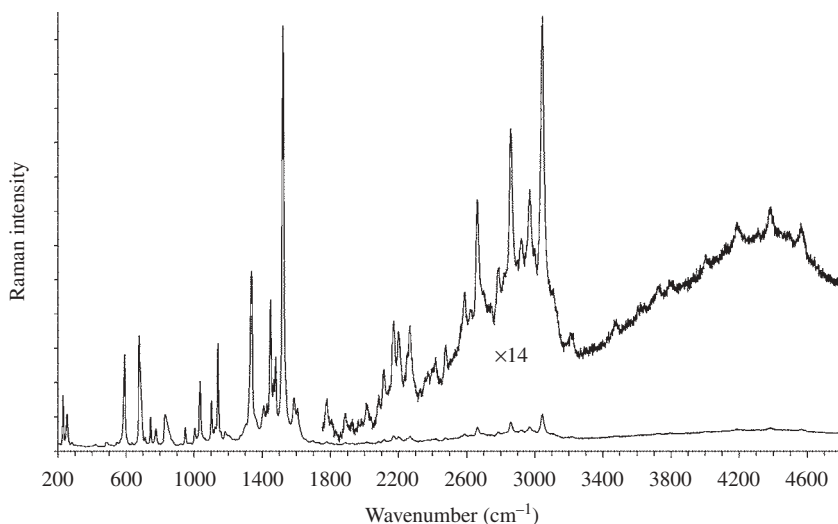


**Figure 4.11.** The spectrum of copper phthalocyanine taken with four different excitation frequencies.

It should be noticed that there are strong similarities between these vibrations and the porphyrin system. This is perhaps not surprising since both contain ring systems which in their simplest form are of  $D_{4h}$  symmetry. On an initial glance, the Raman spectra of phthalocyanines can appear quite similar. For example, the frequency of the band assigned at  $\nu_3$  here is affected by the size of the metal ion. For many metal ions the frequency is linearly dependent on size but for particularly big metal ions, the frequency is lower. This is believed to be because the largest ions can no longer fit into the plane of the ring and exist above or below the plane, allowing displacement to occur more easily. The NIR FT Raman spectra showing this effect are discussed in Section 5 of Chapter 6. The spectra show the band shift when metal-free, copper, gallium and titanium oxy-phthalocyanines were examined.

In Figure 4.11, the effect of changing the excitation frequency on the resonance Raman scattering from copper phthalocyanines can clearly be seen. In this case, and in contrast to the heme system, there are two allowed bands in the visible region, one in the blue and one in the red. There are also weaker bands which could give B-term enhancement by mixing with an allowed band. The band  $\nu_3$  dominates the spectrum at all frequencies, even in the near infrared. However, if the spectra are inspected more closely, it is clear that each spectrum is different due to selective enhancement from resonance with different electronic states.

Finally, the overtones, which were so strong with A-term scattering from small molecules, also occur with heme and phthalocyanine systems. However, despite the presence of some A-term enhancement, they are much weaker, reflecting the smaller displacements of the nuclei during the vibration. Figure 4.12



**Figure 4.12.** Overtone of copper phthalocyanine taken with an excitation frequency of 514 nm.

shows this for copper phthalocyanine. The most intense band corresponds to two quanta of the most intense fundamental band which is assigned as  $\nu_3$  and has  $A_{1g}$  symmetry.

## 4.5 CONCLUSIONS

Resonance Raman scattering will not be effective for all molecules which are coloured. Much depends on the relative efficiency of the scattering and fluorescence processes. Fluorescence can easily dominate the spectra making it very difficult to obtain the Raman scatter experimentally. Sample decomposition and difficulties with self-absorption are also problems. However, for many systems the scattering is strong and there are strategies available to get round the worst interferences. These include the use of pre-resonance to avoid the worst problems with fluorescence and the use of spinning sample holders or flow cells to reduce photodegradation. There are key advantages in using resonance Raman scattering which make it worthwhile. It provides more intense spectra and consequently can be used to selectively pick out and positively identify a molecule in a matrix. Electronic information about a molecule, can be obtained from the intensities of the bands found in resonance, from the energy separations in overtone progressions, and from the overtone patterns that can be obtained. The weak nature of ordinary Raman scattering from molecules such as proteins and in particular water, make it possible to examine resonance Raman scattering directly in the presence of some other materials. This makes resonance Raman scattering a particularly useful form of Raman spectroscopy in biological systems.

## REFERENCES

1. T.G. Spiro and X.-Y. Li in: *Biological Applications of Raman Spectroscopy*, T.G. Spiro (ed.), vol. 3, Wiley, New York, 1988, p. 1.
2. S.Z. Hu, K.M. Smith and T.G. Spiro, *J. Am. Chem. Soc.*, **118**, 12638 (1996).

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## Chapter 5

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# Surface-Enhanced Raman Scattering and Surface-Enhanced Resonance Raman Scattering

### 5.1 INTRODUCTION

Raman microscopists can obtain effective Raman scattering from very small amounts of solid material. Consequently Raman spectroscopy can be said to be sensitive in some circumstances for some solid materials, but for many applications such as analysis in solution, lack of sensitivity remains one of the key limitations. Thus, a Raman technique which could offer a major improvement in sensitivity would be valuable. Surface-enhanced Raman scattering (SERS) gives an enhancement of up to about  $10^6$  in scattering efficiency over normal Raman scattering, but its potential has until now been largely unfulfilled because of the complexity of the technique and problems with understanding the theory. Other techniques such as resonance Raman scattering are better understood and do provide a significant improvement in sensitivity but all have severe limitations. For example, with resonance Raman scattering, the technique is effective only for some coloured molecules and the problems of fluorescence interference and sample photodegradation can limit its use still further. The fact that SERS is effective with a wider range of molecules and gives a bigger enhancement in sensitivity makes the technique worth considering for some targets.

Recently, an increasing amount of work has been published on the use of SERS with analytes which have resonant chromophores. This technique is called surface-enhanced resonance Raman scattering (SERRS) and it has



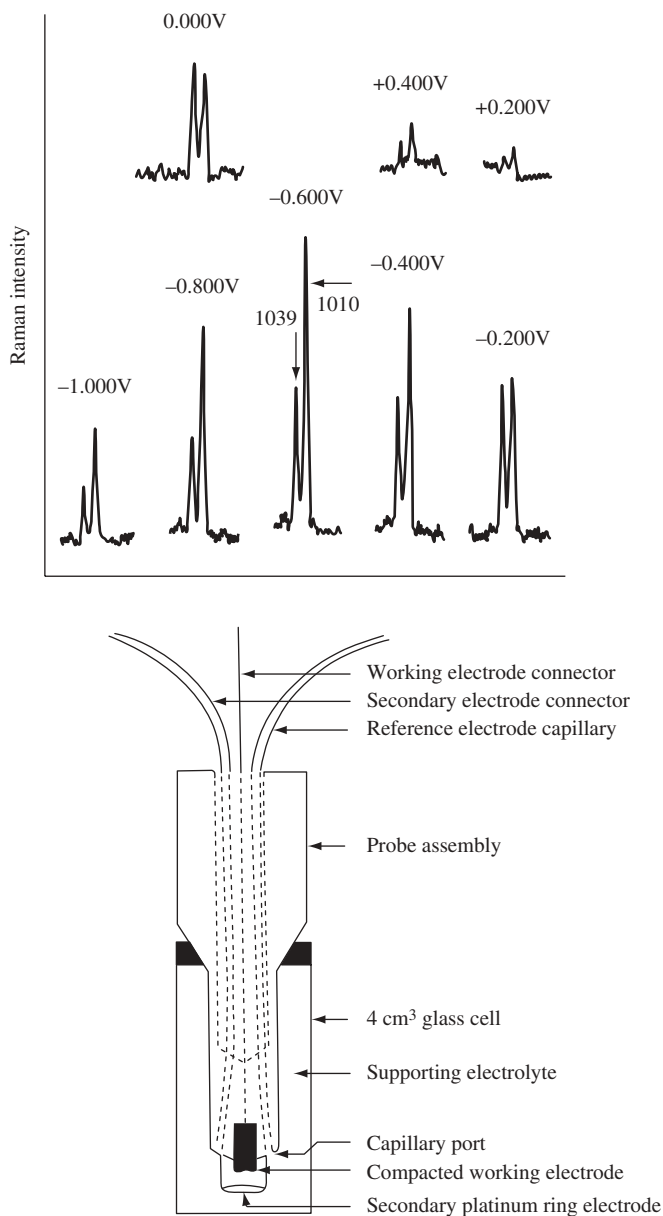
several advantages over SERS. Compared to SERS, it shows a considerable increase in enhancement, and has the sensitivity to rival or surpass that achievable with fluorescence. When a molecule with a chromophore which fluoresces is adsorbed on the SERS active metal surface, the fluorescence is almost completely quenched. As a result, the technique applies to a wider range of molecules than resonance Raman scattering or fluorescence, and molecules normally considered to be fluorophores can be detected by SERRS. Further, the *in situ* identification of a particular molecule from particular features in a spectrum is often much more certain with SERRS. For these reasons, SERRS, though underdeveloped, is now of potential interest as a probe to provide informative detection in areas such as bioanalysis and nanotechnology.

SERS was initially observed in 1974 by Fleischman *et al.* [1]. They reported strong Raman scattering from pyridine adsorbed from an aqueous solution onto a silver electrode roughened by means of successive oxidation–reduction cycles. The authors attributed the effect to a large increase in the electrode surface area caused by the roughening process which enabled more pyridine molecules to be absorbed on the surface. However, Jeanmarie and Van Duyne [2] and Albrecht and Creighton [3] showed that the intensity was due to more than the increase in surface area. They noted that the likely increase in intensity from the roughening of the surface would be less than a factor of 10, whereas the enhancement obtained was of the order of  $10^6$ .

The basic technique consists of using an electrochemical cell into which is placed a solution of the analyte. A possible cell for use in these experiments is shown in Figure 5.1 (bottom). This cell is designed to fit into a glass cuvette and to position the working silver electrode in such a way that the scattered radiation from it is easily focussed into the spectrometer. It is not a particularly efficient electrochemical cell due to the position of the secondary electrode being dictated by the desire to leave the scattered radiation path unobstructed. There are many such designs which in different ways accommodate the conflicting demands of electrochemistry and radiation collection. The spectrum of pyridine taken with different voltages applied to the cell is shown in Figure 5.1 (top). The magnitude of the surface enhancement and the relative intensities of the peaks change depending on the voltage applied.

It has been demonstrated that silver is a particularly good substrate for SERS but some other metals are also effective. Gold is widely used and copper is known to give good enhancement. Other metals including lithium and sodium have also been shown to work well. Many different roughened surfaces have been prepared, the most common being aggregated colloidal suspensions, electrodes and cold deposited metal films including silver island films and silver coated beads.

A number of requirements need to be met for the surface to be SERS-active. It is essential that there is effective surface adsorption of the analyte. Often this is neglected and as a result, poor, variable results are obtained. In addition,



**Figure 5.1.** An example of a simple electrochemical cell for SERS and the spectra of pyridine at various potentials given as relative to SCE. Peak positions are in cm<sup>-1</sup>.

SERS experiments can be carried out in a wide range of environments. These can vary from an atmosphere-controlled vacuum chamber containing small amounts of pure analyte to cuvettes open to the air and containing biological media as well as the analyte. It is possible to make a rough surface of iron and get some surface enhancement, but usually iron has been found to be ineffective. Copper metal gives very effective SERS in some reported studies and not in others. The common reason for failure with both these metals is that the roughened surfaces rapidly form multilayers of oxide in the presence of oxygen. This alters the nature of the surface and can lead to annealing and loss of surface roughness. Further, the distance between the metal surface and the outside of the oxide layer can act as a barrier spacing the analyte away from the actual silver metal and reducing SERS. Only a few authors have fully described the chemical precautions they took in defining the surfaces. The effect of bubbling oxygen or nitrogen gas through solutions has been shown to have a considerable effect on SERS due to a chemical or a physical effect or a combination of the two. Thus, before beginning an SERS experiment it is essential to make sure that the chemistry is controlled and defined. Once this is ensured, it is also necessary to choose the correct metal and roughen the surface appropriately. The following section explains the reasons for this.

## 5.2 THEORY

Since this technique was discovered experimentally, many theories were proposed, particularly in the early stages. To some extent almost all of them contain an element of truth. The problem is that our ability to describe theoretically the bonding or adsorption of an organic molecule to a roughened, probably corroded and oxidized metal surface in water is very limited. In essence most authors now accept that there are two parts to the theory and that both have some validity. This provides a working theory which enables experimental work to proceed with little controversy over the nature of the effect. However, as we will see later in this chapter, the true nature of the theory is still a very active research field. It is likely that the SERS effect is due to one single cause and possible that once the adsorption/complexing process on the surface is better understood, a unified theory will be obtained which will incorporate most of the features of the two theories currently used.

Before briefly describing the theory, it is necessary to understand the nature of the roughened metal surface. Silver surfaces, like the surfaces of other metals, are covered with electrons. They arise from the conduction electrons held in the lattice by the presence of positive charge from the silver metal centres. At the surface, the positive charge is only on the metal side of the electrons. Consequently the electron density extends a considerable distance from the surface and there is also freedom of movement in a lateral direction along it. When a light

beam interacts with these electrons, they begin to oscillate as a collective group across the surface. These oscillations are termed surface plasmons.

Surface plasmons from small uniform particles, or from surfaces which have a single periodic roughness feature, have a resonance frequency at which they absorb and scatter light most efficiently. The frequency varies with the metal and the nature of the surface. It so happens that both silver and gold plasmons oscillate at frequencies in the visible region and therefore, they are suitable for use with the visible and NIR laser systems commonly used in Raman scattering. On a smooth surface the oscillation occurs along the plane of the surface. Absorption can occur but no light will be scattered. To get scattering, there needs to be an oscillation perpendicular to the surface plane and this is achieved by roughening the surface. This locates the plasmon in the valleys of the roughened metal surface and scattering is caused as the plasmons move up to the peaks. These peaks from which scattering is deemed to occur are sometimes called 'lightning rods'.

Other features of the metal are vital. First, metals can both scatter and absorb but the ratio of the two is metal-dependent and, compared to other metals, the ratio for silver favours scattering. To a physicist, the dielectric constant of the metal is divided into two parts, the real and imaginary. Scattering is associated with the real part and absorption with the imaginary part. Some of the SERRS papers use this terminology but it is largely beyond the scope of this book; however, further information can be found in reference [4].

In addition to the ratio of absorption to scattering, the nature of the roughness is important. Usually for a metal surface obtained either by electrochemical roughening of the electrode or by depositing silver onto a surface, there are many different roughness features of varying dimensions. The result of this is that the plasmon on the surface usually covers quite a broad range of wavelengths. It is simple to determine this by measuring the absorption spectrum of the plasmon. However, with nearly mono-dispersed colloids, the range of frequencies covered by the absorption band is very much narrower and usually the half-width is about 50–60 nm indicating a much more defined surface roughness.

Thus, to obtain good SERRS, the surface must be reasonably clean or at least must not form too thick an oxide layer, and it must be suitably roughened in a way that is time-stable. In addition, it needs to be of a material that has plasmons which resonate in a frequency range which includes that of the exciting laser. The basics of how this is believed to give effective SERS is given in Section 5.3.

### **5.3 ELECTROMAGNETIC AND CHARGE TRANSFER ENHANCEMENT**

There are two different theories of surface enhancement which are currently used [4–7]. In one, the analyte is adsorbed onto or is held in close proximity to

the metal surface, and an interaction occurs between the analyte and the plasmons. This is called electromagnetic enhancement. In the other, the adsorbate chemically bonds to the surface. Excitation is then through transfer of electrons from the metal to the molecule and back to the metal again. This is called charge transfer or chemical enhancement. By definition it can only be possible from the first layer of the analyte attached to the surface whereas electromagnetic enhancement could occur from a second or subsequent layer. Some enhancement has been claimed up to about 20 Å or more away from the surface.

### 5.3.1 Electromagnetic Enhancement

The simplest description of electromagnetic SERS is based on models of a small metallic sphere. This is clearly not going to be adequate since there is no roughness of the type found to be important experimentally. For example, the simple sphere could be regarded as a first approximation to a single colloidal particle but we know that aggregation of suspensions of these particles gives much increased SERS. However the sphere model can be used to explain much of the basic process. The effect of aggregation can be dealt with after consideration of the sphere model.

When a small metal sphere is subjected to an applied electric field from the laser, the field at the surface is described by

$$E_r = E_0 \cos \theta + g \left( \frac{a^3}{r^3} \right) E_0 \cos \theta \quad (5.1)$$

$E_r$  is the total electric field at a distance  $r$  from the sphere surface,

$a$  is the radius of the sphere,

$\theta$  is the angle relative to the direction of the electric field,

$g$  is a constant related to the dielectric constants such that,

$$g = \left( \frac{\epsilon_1(\nu_L) - \epsilon_0}{\epsilon_1(\nu_L) + 2\epsilon_0} \right) \quad (5.2)$$

$\epsilon_0$  and  $\epsilon_1$  are the dielectric constants of the medium surrounding the sphere and of the metal sphere respectively.  $\nu_L$  is the frequency of the incident radiation.

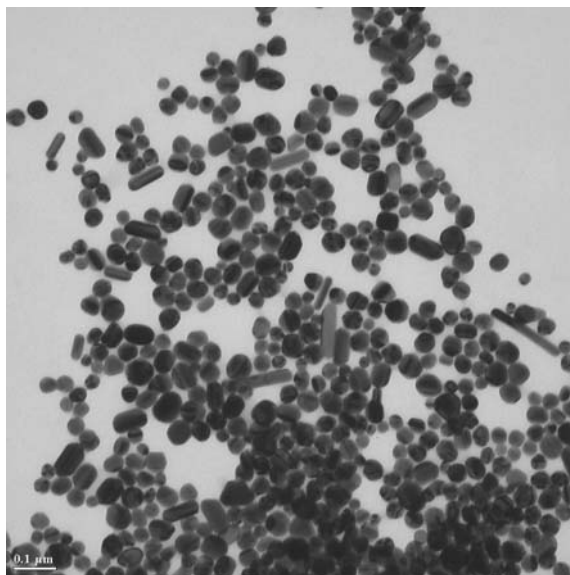
At some point where the denominator is at a minimum, the value of  $g$  will be a maximum.  $\epsilon_0$  is usually close to 1 and consequently this maximum usually occurs when  $\epsilon_1$  is equal to  $-2$ . At this frequency, the plasmon resonance frequency, the excitation of the surface plasmon greatly increases the local field experienced by the molecule absorbed on the metal surface. In essence, the molecule is bathed in a very freely moving electron cloud and that movement

intensifies the polarization of the surface electrons. The electrons in the analyte molecule adsorbed on the surface interact with this cloud causing greater polarization around the molecule.

At the metal surface the total electric field is averaged over the entire surface of the small sphere. At any point on the surface the electric field may be described by two components, the average field perpendicular to the surface and the average field parallel to the surface. Clearly,  $g$  is dependent on the dielectric constants of the metal and the surrounding medium and also the laser frequency. Since the dielectric constant of the metal is generally about 1, it can be seen by substituting this into Equations (5.1) and (5.2), that the electric field is greater perpendicular to the surface than parallel to it. Thus, the greatest enhancement is observed for a molecule adsorbed on the surface and polarized perpendicular to it. Further, since the field is inversely proportional to  $r^3$ , the magnitude of the SERS enhancement drops off rapidly with distance from the surface.

It is now known from many experiments, mainly on small particles adsorbed on a surface, that the greatest enhancement does not occur evenly round every isolated particle but at points between some touching particles or clusters of particles. Enhancement from single particles has been observed, particularly for SERRS. However, the greatest enhancement occurs from interactions between particles. When silver nanoparticles are adsorbed onto a surface to form a layer, it is possible to study the distribution of enhancement across the surface. With any appropriate laser frequency, some parts of the surface become extremely active and other parts remain inactive. These active parts are called 'hot spots' and the regions which are active depend upon the excitation frequency used. It can be shown that the particularly active sites are at points between particles. The precise reasons for this are still the subject of research but the basic reasons are contained in the simple theory already described. Each individual particle will have a plasmon for which the resonance condition is only satisfied by a small range of wavelengths. However, the electrons are only loosely held and are free to couple to adjacent particles so that the plasmon is actually the plasmon of more than one particle and will have a new frequency range over which resonance can occur. The actual frequency of the plasmon for single particles decreases as the particle size rises and similarly dimers, trimers, etc., of particles have plasmon resonances at lower frequencies. The point at which two particles touch will generate enormous electric fields so that points of contact will give particularly effective SERS. Other more localized features may also contribute large amounts of scattering to the total. Thus, the low frequency chosen, the particle size and shape, and the way the particles organise in clusters will also contribute to the SERS enhancement.

Figure 5.2 shows a TEM of a typical colloid used in these experiments. It can be seen that there is a variation in particle size and that there are a number of particle interactions caused by the way that this material has been dried onto



**Figure 5.2.** A typical colloid used in SERS. It was prepared by citrate reduction of silver nitrate and shows some needles which occur in some but not all preparations.

the surface. In some practical applications suspensions of colloidal particles are used so that scattering from many particles are detected and averaged.

### 5.3.2 Charge Transfer

Charge transfer or chemical enhancement [7] involves the formation of a bond between the analyte and the metal surface. This bond is believed to produce a surface species which includes the analyte and some surface metal atoms. This makes it possible to transfer charge (electrons or holes) from the metal surface into the analyte. The formation of this surface species will increase the molecular polarizability of the molecule considerably due to interaction with the metal electrons. Basically, the enhancement is thought to proceed via new electronic states which arise from the formation of the bond between the analyte and the metal surface. These new states are believed to be resonant intermediates in the Raman scattering. Thus, as opposed to the radiation being absorbed or scattered through the plasmons on the surface, the radiation is absorbed into the metal. A hole is transferred into the adsorbate metal atom cluster, the Raman process then occurs, excitation is transferred back into the metal and re-radiation occurs from the metal surface.

There is evidence for both these theories. However, it is very difficult to differentiate them. Clearly, chemical enhancement should occur only from

molecules directly attached to the surface and consequently should increase only up to monolayer coverage. However, electromagnetic enhancement, although a longer range effect, drops off as  $1/r^3$  with distance from the surface. Thus, most of the electromagnetic enhancement will also arise from adsorbates present on the surface up to monolayer coverage. The vast majority of evidence points to both effects having a part to play although it is generally believed that electromagnetic enhancement may have a greater part to play than charge transfer enhancement.

## 5.4 SELECTION RULES

SERS spectra are not straightforward to interpret. New peaks which do not appear in normal Raman scattering can appear in SERS and some peaks which are strong in normal Raman scattering can become very weak or disappear altogether. In addition, the intensity changes which occur at different concentrations can be nonlinear. A classic example of this is with pyridine. Well below monolayer coverage, the pyridine spectrum is very weak but it becomes quite strong as monolayer coverage is approached. At low concentrations the molecules are present on the metal surface with the plane of the pyridine ring parallel to the plane of the surface. As the concentration increases the plane of the pyridine ring is forced into an orientation perpendicular to the surface to allow more molecules to pack. This causes a rapid rise in SERS intensity. The reason this alters the intensity of SERS has already been discussed in general when it was stated that one requirement for scattering is that there is a polarizability component perpendicular to the surface. When light interacts with the surface, the effect can be described by two electric dipole components parallel and perpendicular to the surface. It is molecular polarizability caused by the perpendicular component which leads to scattering from the rough surface. For pyridine, the plane of the ring will produce the greatest polarizability changes. Thus, if the molecule is lying with the plane parallel to the surface, most of the polarizability change will be parallel to the surface and consequently will not contribute to scattering. When the plane is perpendicular to the surface the scattering process will be efficient.

The appearance of new bands further complicates the assignment. The most common reason this occurs is when a molecule has a centre of symmetry. Adsorption of the molecule onto a metal surface will effectively break the centre of symmetry. This results in the mutual exclusion rule (see Chapter 1) no longer being applicable, allowing some of the infrared active bands to break through and appear in the SERS spectrum. However, the situation is more complex than that. Some types of bands are naturally more intense in SERS than they are in normal Raman scattering. An example of this will be shown in Chapter 6. A consideration of the main effects led Creighton [6] to propose



selection rules which work well in most circumstances. In theory they refer to electromagnetic enhancement but seem to be applicable in many cases. The problem with chemical enhancement is that the nature of the species formed between the adsorbate and the surface is not clearly defined. In principle, the selection rules should refer to the surface species including the molecule and the metal atoms complexed to it. However, in practice, considering the molecule as a distinct entity and ignoring the effect of the metal atoms other than the change they cause in molecular symmetry appears to be effective in most cases. These simple selection rules have proved to be useful in determining the orientation of a molecule on the surface and explaining some of the differences between SERS spectra and normal Raman spectra. However, there is still much to be learned about the reasons for the intensities of SERS active bands.

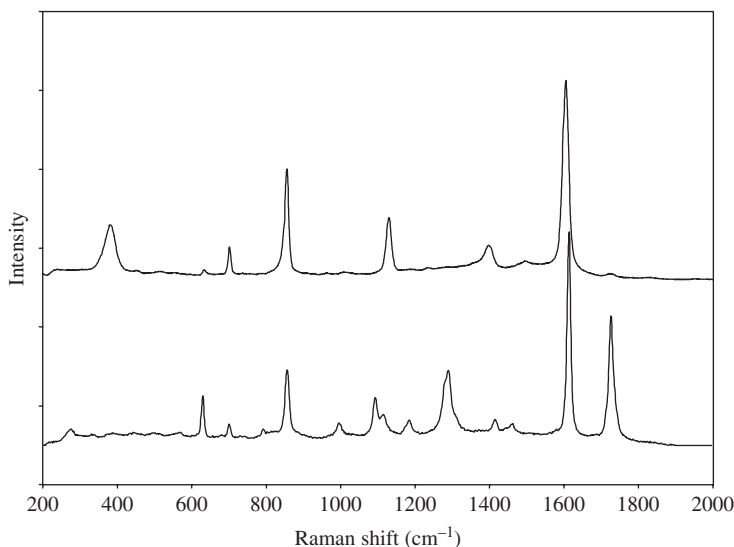
The fact that there are selection rules is a problem in SERS. The appearance of new bands and the disappearance of existing ones makes it much more difficult to relate the spectra obtained on the surface to that obtained from normal Raman scattering. In addition, since the sensitivity of SERS compared to normal Raman scattering is huge (a factor of  $10^6$ ), the dominant features of the spectrum could arise from a contaminant which sticks strongly to the surface. These problems make positive assignments difficult. Overcoming this difficulty is one of the key advantages of SERS. However, before going on to explain the advantages and disadvantages of SERS, a few applications of SERS are discussed.

## 5.5 APPLICATIONS OF SERS

SERS is one of the very few methods which can give effective, molecularly specific information about an adsorbate on a metal surface, *in situ*, in aqueous solutions. It has been applied to the detection of many molecules. For example, benzotriazole is widely used as an anti-corrosion agent for copper and an anti-tarnish agent for silver. Therefore the detection of the formation of the surface layer and elucidation of the nature of the surface complex are of considerable commercial importance. Roughened copper or silver surfaces treated with benzotriazole give very good SERS spectra which can be assigned positively to benzotriazole. The approximate orientation of the molecule and something about the nature of the complex it forms can be deduced. Of course, effective SERS is obtained only from certain surfaces of some metals and, as referred to earlier, even for some effective metals such as copper, it is difficult to study the surface reactions because of the rapidly changing nature of the copper surface in the presence of oxygen. One way of extending SERS to other surfaces is to add silver colloid to the surface of another metal which had been treated previously to form a surface layer of an organic molecule. This causes contact between the organic layer and the silver and does give effective spectra. However,

it is difficult to assign the spectra and relate it to the structure of the organic surface layer, as it may not be clear whether the organic adsorbate remains attached to the original SERS-inactive surface or transfers to the silver surface. Thus, although the technique is simple, the interpretation requires careful consideration.

It is also possible to detect SERS from a non-metallic material. SERS from the surface of the polymer polyethylene terephthalate (PET) is of interest because it is often surface-treated with other polymer layers. Good SERS are obtained when a thin film of silver is deposited on the surface and the silver film irradiated from the side away from the polymer so that the radiation strikes the silver first. The spectra (Figure 5.3) are different from the Raman spectra, indicating the effect of surface selection rules on the spectrum. In particular, the band above  $1700\text{ cm}^{-1}$ , which is due to the carbonyl group in the Raman spectrum, is weaker in the SERS spectrum and in addition new bands appear. However one of the most notable features of this spectrum is the fact that it is taken by irradiating and collecting from the silver side away from the polymer. Since silver is a good absorber of visible light, no appreciable exciting radiation should penetrate the film into the polymer. Further, no weak Raman scattered light formed as a result of any breakthrough should be transmitted back through the silver. This appears to be the case in practice. Bands strong in



**Figure 5.3.** SERS spectrum of polyethylene terephthalate (PET) taken from a sample with a silver film cold-deposited on the surface (top) compared to a Raman spectrum of the same sample (bottom). SERS was recorded using excitation was from the side of the silver film away from the polymer layer.

normal Raman scattering from the polymer and weak in SERS do not appear except at the intensity expected for SERS. The reason this works is that the effective silver film is thin (approximately 15 nm) and the plasmon is much larger than this so that it transcends the film and is operative on both sides. Thus an interaction between the molecule and the plasmon on one side of the film can be detected on the other side. This results in only the surface layer in contact with the silver being enhanced and not the bulk of the polymer. Obtaining spectra from a very thin surface layer is difficult using simple techniques so that this is valuable information. In addition this example illustrates two key features of SERS which were discussed in the theory section. There are different selection rules compared to Raman scattering and there is definite coupling of the SERS-active species to the plasmon.

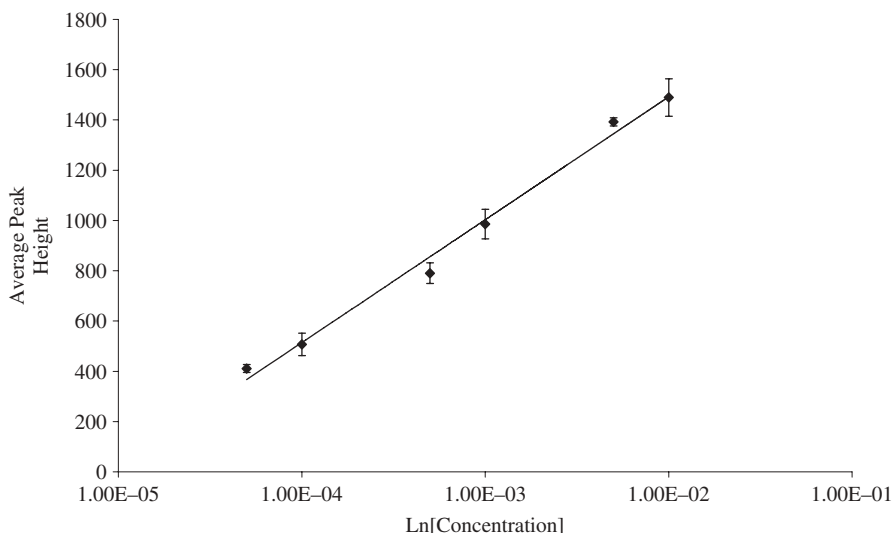
Another possible use for SERS is as a detection system in chromatography. An electrode can easily be placed in the line and can be cleaned by recycling and recreating the roughened surface after every determination. Provided the analyte or a suitable derivative adsorbs strongly on the metal surface, sensitive detection is possible. Alternatively, a flowing stream of colloid can be mixed with the effluent from the chromatography column and the stream passed through a capillary. The signal is then detected by irradiation and collection of the scattered light from the side of the capillary. However, there are major problems with SERS detection. With electrochemistry, it can be difficult to replicate the roughness on the electrode surface each time and, in the case of colloid, batch to batch reproducibility and control of the aggregation state are difficult. The colloidal technique is proving in practice to be more sensitive, and considerable efforts are being devoted to obtaining greater reliability.

With careful control, colloid can be made repeatably to a particular specification and TEMs indicate this colloid can be close to mono-disperse. Provided the colloid is time stable, a standard can be used to calibrate out variations in the assay and so a degree of quantitation is possible. However, only molecules which adhere to the surface will be active. The main problem is controlling the state of aggregation of the colloid. In essence, the colloid is stable because of the surface charge on the particles. Commonly, the aggregating agent added reduces this charge and causes controlled aggregation. This shifts the plasmon frequency so that some aggregates are in resonance with the laser but remain in suspension. The agents used vary from inorganic compounds such as sodium chloride to organic compounds such as poly-L-lysine. They work either by reacting with the surface, as in the case of sodium chloride which forms a silver chloride layer on the surface, or simply by coating the surface as is the case with poly-L-lysine. This produces less stable colloid and causes aggregation. It is a dynamic process that continues with time. However, in practice, it is possible to produce suspensions which are sufficiently stable to give time-stable SERS for periods of up to several hours in some cases. Given that the SERS measurement is very sensitive, and accumulation times of 10 s are

normal, this should be adequate. However, it is important that this aggregation process is controlled as effectively as possible. One way this has been done is by using a flowcell. In this system the colloid flows down one tube and the aggregating agent down another. Once thoroughly mixed the analyte is added down a third tube to the aggregated colloid and the flowing stream is interrogated by the Raman spectrometer. In this system, relative standard deviations of less than 2% can be obtained and the system is sufficiently quantitative for regular use.

Given that we know that the enhancement from each molecule may well be different, the reason this technique can give quantitative results is because it averages over many molecules and many hot spots. A very different effect is found when very small numbers of molecules are present. At this point, the Raman signal does not remain constant during accumulation of the scattering. Every time a hot spot with an adsorbate on it passes through the beam, a burst of scattered light is recorded. This process has some similarities to true single molecule detection where signal 'blinking' is observed but it is more about single aggregate detection. Thus, claims of single molecule detection by this technique alone should be treated with some reserve unless well supported by other evidence.

Because of the averaging effect, a good analyst can obtain quantitative information from SERS. Figure 5.4 shows the results of the addition of amphetamine to a colloidal suspension aggregated with sodium chloride. As



**Figure 5.4.** SERS from amphetamine added to a colloidal silver suspension aggregated with sodium chloride. (Reproduced with permission from K. Faulds, W.E. Smith, D. Graham and R.J. Lacey, *Analyt*, **127**, 282 (2002).)

can be seen, the results are quantitative over two orders of magnitude and provide a sensitive method of detecting amphetamine in solution.

Thus, if SERS is to be used as a detection technique, a careful consideration of the chemistry of the surface and the physics of surface enhancement is required; but with care and by using the technique within its limitations, good quantitative measurements can be obtained. Overall, the difficulties with SERS have certainly limited its application. However, the related technique of SERRS has fewer problems and such unique properties that it is likely to become an important analytical method for the solution of specific problems.

## 5.6 APPLICATIONS OF SERRS

As stated above, SERRS combines the advantage of surface enhancement with the use of a resonant chromophore so that molecular resonance enhancement as well as surface enhancement is obtained. In this method, a dye or a molecule containing a dye is used as the analyte. The enhancement obtained is probably due to one single process and cannot be explained simply by adding molecular resonance and surface enhancement together. For example enhancements of up to  $10^{14}$  have been claimed rather than  $10^8$  or  $10^9$  and users certainly experience much greater sensitivity with it than would be expected simply from the addition of molecular resonance to SERS. Having said this, it is easier experimentally to treat the effect as being due to a combination of the two known effects; provided the previous caveat is borne in mind, this works well. There are a number of reasons why the technique is effective. The absorption of the dye directly onto a metal surface causes all fluorescence to be quenched. This is a very efficient mechanism, more efficient than that of standard molecular quenchers, and consequently both fluorescent and non-fluorescent dyes can be used as analytes or as part of analytes.

The signals obtained from SERRS often resemble quite closely those obtained from resonance Raman scattering with much less evidence of orientation dependence or other surface selection rules. Normally, the relative intensities of bands in the SERRS spectrum and in the resonance spectrum may differ by up to 30% but any frequency shifts are very small. Thus, normally it is easy to recognize a particular adsorbate in SERRS simply by comparing it with the resonance Raman spectrum or, in the case of a fluorescent compound, the FT Raman spectrum with the SERRS spectrum. Further, there is less of a problem with contaminants since the additional resonant enhancement discriminates against many of them. Finally, the additional enhancement often means that lower laser powers and shorter accumulation times can be used. Consequently surface photodecomposition is much less of a problem.

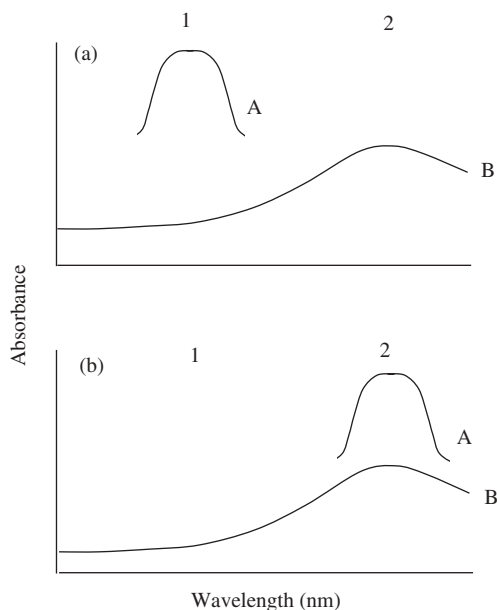
The increased reliability with which a species can be positively identified provides increased confidence when measuring at very low concentrations that the signals obtained do come from the analyte. This in no way means that contamination is no longer a problem with the technique. All extremely sensitive analytical methods suffer from the possibility that other molecules may be present in extremely small quantities; for example, adsorbed on a vessel wall from a previous experiment, from rubber gloves, or from seals or stoppers. However, the fact that they can be instantly recognized is a significant advantage over most other ultrasensitive techniques, and leads to confidence in the reliability of SERRS.

## 5.7 THE BASIC METHOD

Ideally, the analyte should be a dye which has an absorption maximum at or close to the frequency of the plasmon resonance on the active surface. In this way both molecular resonance and surface plasmon resonance are obtained. In practice this is not always possible or, in some cases, even desirable. However, it appears in practice that an exact match is not required. Figure 5.5 shows a simple diagram explaining the different ways in which SERRS can be obtained. In Figure 5.5a the plasmon band and the absorption band are at the same frequency and so the excitation should be chosen to be close to that frequency. In Figure 5.5b the absorption band and the plasmon band are at different frequencies and the choice would have to be made as to whether to choose the excitation frequency at the frequency of the plasmon resonance, at the frequency of the molecular resonance or in between.

Using colloidal silver as substrate, SERRS has been recorded from a non-aggregating dye with no aggregating agent. The SERRS must come from single particles and consequently does not include any enhancement from hot spots or particle/particle interactions. Nevertheless, in contrast to SERS the signals are quite strong. The strongest signals were obtained at the plasmon resonance maximum, with much smaller signals obtained at the dye absorption maximum. It would appear that for single particle excitation, the frequency chosen would be that of the surface plasmon.

With an aggregating dye, the absorption maximum in the electronic spectrum at the plasmon frequency of the single particle is reduced and a broad absorption at longer wavelengths grows in. This is due to the formation of a range of species including dimers, trimers and a range of clusters of different sizes. Each of these species has a separate absorption maximum and the broad band is a combination of absorbances from each of them. At any one of these frequencies, some but not all of the aggregated species will have a plasmon which is in resonance and so these species contribute significantly to the enhancement. In this case, the combination of surface enhancement and

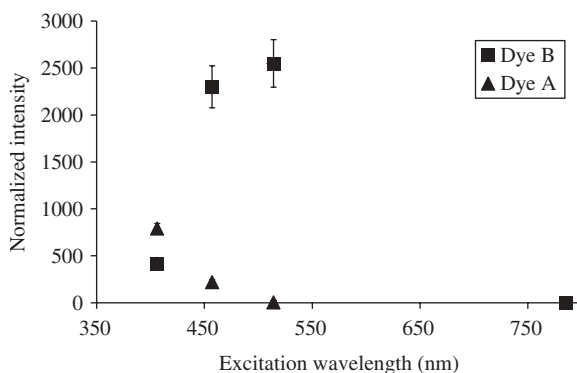


**Figure 5.5.** Different combinations of plasmon resonance (B) and absorption band (A) arrangements for SERRS. (Reproduced with permission from C. Rodgers, W.E. Smith, G. Dent and M. Edmondson, *J. Chem. Soc. Dalton Trans.*, 791 (1996).)

resonance enhancement extends over a range of frequencies. In practice this is a range up to 150 nm or so from the molecular resonance frequency above which the enhancement tails off to the level expected for SERS.

Figure 5.6 shows a plot of the intensity of a major peak from two similar azo dyes, one which does not cause aggregation (dye A) and one which does (dye B). The absorption maxima of the dyes were 429 and 442 nm, respectively, and the absorption maximum of the colloid unaggregated was 404 nm. Dye A contains a hydroxyl group which ionizes at neutral pH to give a negative ion. When adsorbed on the surface this helps maintain the negative charge of the particle and prevents aggregation. Dye B displaces negatively charged material on the surface and reduces the surface charge. With dye A the SERRS intensity was greatest at the frequency of the surface plasmon and dropped off away from it, as expected for unaggregated colloid. Dye B showed greater intensity across the visible region dropping off towards the infrared, as expected for aggregated colloid.

The use of coloured reagents to obtain the extra sensitivity has led to a large number of single molecule experiments. It is reasonably clear now that SERRS has the potential to detect a single molecule and that the molecule can be positively identified in solution. Consequently SERRS has some unique advantages

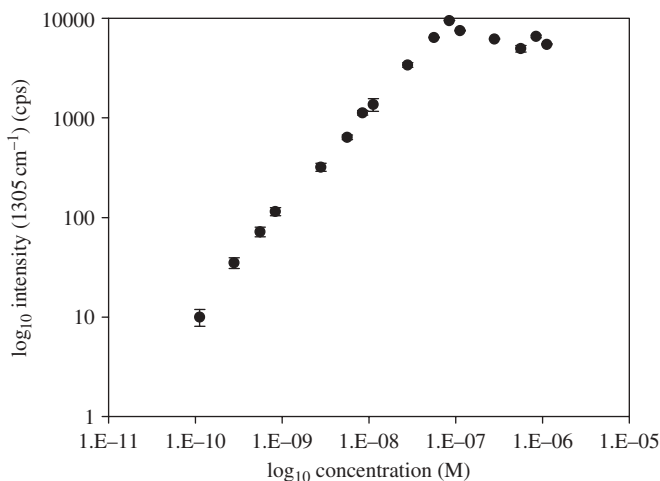


**Figure 5.6.** Plot of the intensity dependence of one peak for both a non-aggregating dye (single particle enhancement) and an aggregating dye (cluster enhancement). (Reproduced with permission from K. Faulds, R. Littleford, D. Graham, G. Dent and W.E. Smith, *Anal. Chem.*, **76**, 5902 (2004).)

for ultra-sensitive analysis. However, it has also been shown that as with SERS, there are hot spots and the greatest enhancement is obtained at points where two nanoparticles touch. In addition, there are several studies which show that, as for SERS, the enhancement appears to be uneven across the surface. Thus, although some of the problems with SERS have been overcome, care must still be taken if reliable representative results or quantitative results are to be obtained. Two examples which give quantitative analysis and illustrate the practical advantages are given below.

The concentration of the coloured anti-cancer drug mitoxantrone is difficult to analyse in blood. It requires quite a complex procedure usually involving separation of the mitoxantrone from the blood serum and chromatography. Using a flow system to control aggregation, a drop of plasma from a patient who had been undergoing a course of therapy with mitoxantrone was added to the flow cell. Not all the plasma would be expected to adsorb on the silver colloid and consequently a fluorescence background might be expected from non-adsorbed material. However, when the flowing stream containing the plasma was mixed with streams containing colloid and an aggregation agent and the mixed material passed across the spectrometer, excellent mitoxantrone spectra were obtained with little evidence of background fluorescence. One reason is that the flow cell causes a significant dilution in the plasma before measurement and this dilutes out the background fluorescence from the non-adsorbed material. However, the mitoxantrone desorbs from the plasma proteins and adheres strongly to the silver surface. Thus, SERRS from mitoxantrone can be obtained within a minute or less directly from serum sample. Figure 5.7 shows results over a range of concentrations. There is good linearity



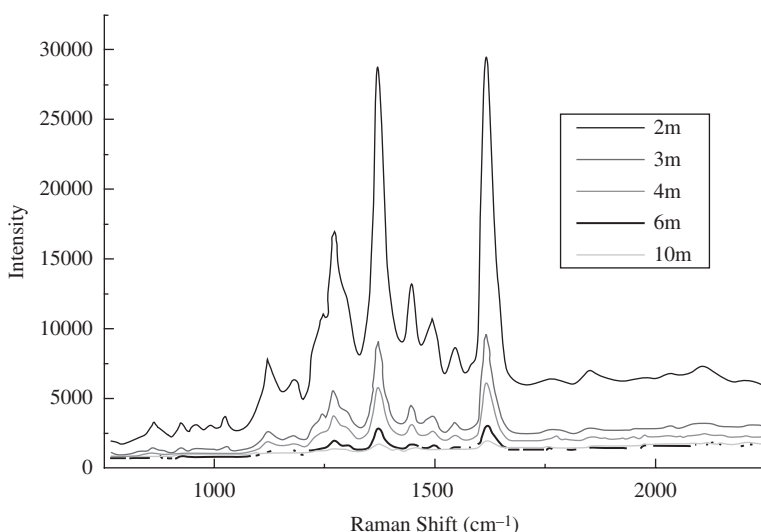


**Figure 5.7.** Intensity dependence of one peak from the SERRS spectrum of mitoxantrone in plasma. (Reproduced with permission from C. McLaughlin, D. MacMillan, C. McCardle and W.E. Smith, *Anal. chem.*, **74**, 3160–3167 (2002).)

over orders of magnitude. This range encompasses the effective concentration range found in patients so that the technique can be used directly. This is an example where SERRS could be considered as the technique of choice. However, this assay used a coloured drug which adsorbed strongly onto the silver surface. Doing this with other drugs could be more difficult.

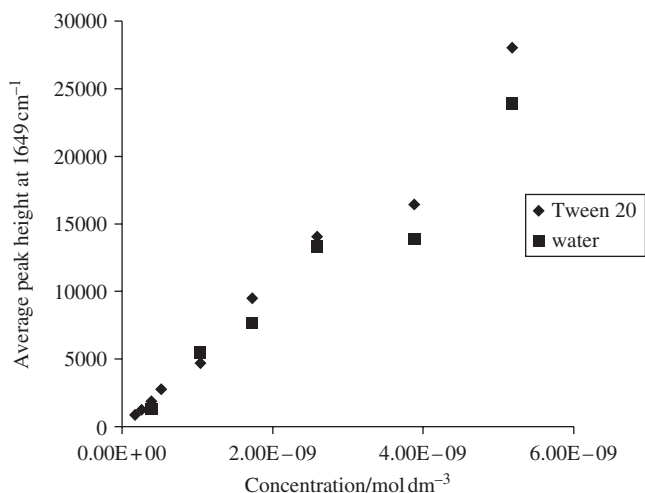
One big advantage of SERRS is that it gives a set of sharp, molecularly specific peaks and therefore it should be relatively simple to differentiate several SERRS-active analytes without separation. For example, this would mean that it would be possible to write codes into a piece of plastic or to detect several DNA strips without separation. Using a simple Raman spectrometer with a telescopic lens and a laser providing 3.6 mW of 532 nm excitation, SERRS was detected at distances of up to 20 m within 10 s. The sample was colloid-treated with a dye and fixed in a polymer. This result is illustrated in Figure 5.8. It indicates that the SERRS sensitivity can be obtained in practice.

With DNA, effective SERS is difficult to obtain since the DNA molecule is negative and most of the colloidal particles used for this type of analysis are also negative. Thus, spectra can be obtained at higher concentrations but not at really low concentrations. In addition DNA replicates the same four bases and a sugar and often it is the characterization of the order of these bases or some defect in one of the many which is required. Consequently sharp information on any one base can be difficult to obtain. The same problem is encountered in other spectroscopies. To overcome this problem, one standard approach is to use sequences of DNA which will recognize the complimentary strand that



**Figure 5.8.** Distance dependence of the SERS spectrum of a dye adsorbed onto silver colloid incorporated in a polymer. (Reproduced with permission from Ailie McCabe, W.E. Smith, G. Thomson, D. Batchelder, R. Lacey, G. Ashcroft and B.G. Foulger, *Appl. Spectrosc.*, **7**, 56 (2002).)

contains the defect. These sequences are labelled with a fluorophore or any other marker. It is the marker which is detected in the analytical procedure. There are advantages in sensitivity and selectivity in using SERRS as the detection technique for these markers. To do this, DNA was modified by the addition of dyes that adsorb strongly onto the silver surface. Initially this was easier to do using fluorophores since they are commercially available coupled to DNA bases for use in fluorescence analysis. Using similar procedures with a standard fluorescence assay, DNA concentrations down to between  $10^{-12}$  and  $10^{-13}$  M could be determined; the results are shown in Figure 5.9 for one sequence. These results were obtained from a suspension of DNA in a cuvette. However, the Raman beam is sharply focussed and consequently only a very small volume of that cuvette is actually used for the analysis. If a calculation is done on how many molecules are present in the beam at any one time, the results indicate that we are at the single molecule sensitivity limit obtained by using a standard commercial spectrometer, normal laboratory methods and an accumulation time of 10 s. Good quantitative SERRS can now be obtained in 100 ms and the limitation here is not the SERRS technique, but the limitations of the instruments used to give quantitative results. Much shorter times can easily be achieved from the huge signals that are now routinely and reliably obtained.

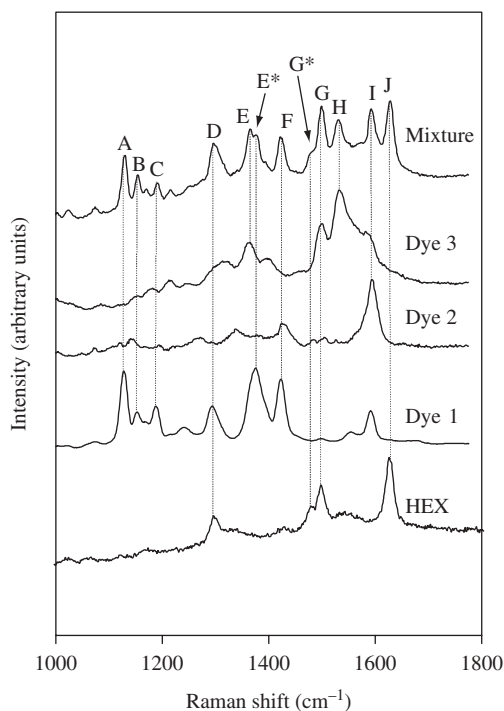


**Figure 5.9.** SERRS concentration dependence of one of eight dye-labelled oligonucleotides.

In one recent experiment, using DNA, eight different fluorophores were attached to DNA strips. From all but one of these SERRS, exhibited a sensitivity three to four orders of magnitude greater than that achieved by fluorescence detection using two standard fluorescence spectrometers. This is a very remarkable result. The SERRS experiment gives the full spectrum whereas the fluorescence method accumulates all the fluorescence through a simple and efficient filter system. It indicates clearly that SERRS has very significant potential for ultra-sensitive detection. It may still be argued by some that SERRS can be variable. In this particular experiment, the data quoted are detection limits which means that we have not only linear gradients but also relative standard deviations at the lowest levels which are better than those achieved through fluorescence, indicating the technique is now reliable and quantitative.

Another remarkable feature of this work is that it was done in a cuvette. Techniques which control aggregation such as flow cells could be used to improve the situation further.

The sharp, molecularly specific nature of the signals is another characteristic of SERRS. It can be used to label colloidal particles so that they are uniquely coded with the mixture. Figure 5.10 shows the result of mixing three different dyes and a dye labelled oligonucleotide together into a suspension of silver colloid. Each dye can be separately identified in the suspension. Of course there is no guarantee that all dyes are on any one particle, but the experiment shows that with further development, SERRS has great potential for coding.



**Figure 5.10.** A colloidal suspension containing three dyes and an oligonucleotide illustrating the ability of SERS to discriminate between labels in solution.

There are no particular secrets in this work. The technology is now relatively simple and readily available. What is important is that both the chemistry of the attachment to the surface and the physics of the measurement must be considered by the analyst.

## REFERENCES

1. M. Fleischman, P.J. Hendra and A.J. McQuillan, *Chem. Phys. Lett.*, **26**, 163 (1974).
2. D.C. Jeanmarie and R.P. Van Duyne, *J. Electroanal. Chem.*, **84**, 1 (1977).
3. M.G. Albrecht and J.A. Creighton, *J. Am. Chem. Soc.*, **99**, 5215 (1977).
4. M. Moskovits, *Rev. Mod. Phys.*, **57**, 783–826 (1985).
5. A. Campion and P. Kambhampati, *Chem. Soc. Rev.*, **27**, 241 (1988).
6. J.A. Creighton, in: *Spectroscopy of Surfaces*, R.J.H. Clark and R.E. Hester (eds), Wiley, 1998, p. 27.
7. A. Otto, I. Mrozek, H. Grabhorn and W. Akemann, *J. Phys. Cond. Matter*, **4**, 1142 (1992).



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# Chapter 6

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## Applications

### 6.1 INTRODUCTION

In the previous chapters, examples of materials examined by Raman spectroscopy have been given to highlight specific aspects of the technique. Whilst the technique was initially used to examine inorganics, it grew with extensive use in polymer analysis. More recently there has been a growth in pharmaceutical applications, while other applications have been successfully established in colours, semiconductors, art, archaeology and biotech areas. There have also been advances in forensic and process analysis. In several areas the ability of Raman spectroscopy to analyse materials in glass, water, inside packaging materials or *in situ* directly has been exploited. This chapter will attempt to show ways in which Raman spectroscopy can be used to solve specific analytical problems. Compared to many other analytical techniques Raman spectroscopy is viewed by many as a niche technique. However the applications are fast growing and in this chapter we can only attempt to highlight the areas where the technique has been successful. Some applications within the authors' experiences are given in more detail to exemplify the strengths and pitfalls of the technique which will act as a guide to the reader's potential use in their own areas of interest.

### 6.2 INORGANICS AND MINERALS

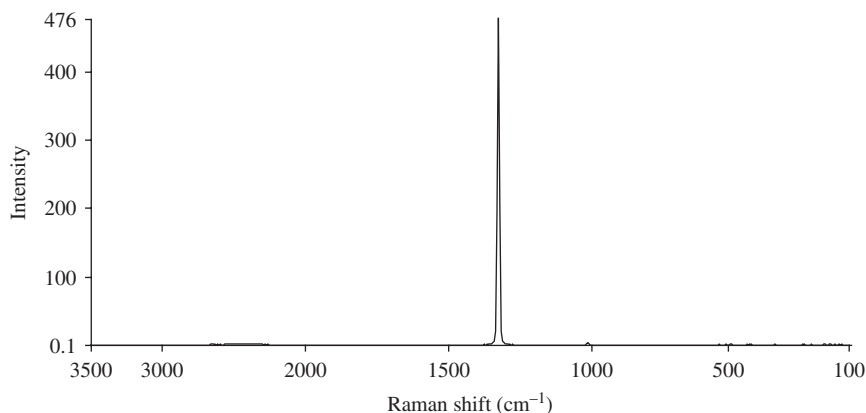
Raman spectroscopy is a very good tool for the examination of inorganic materials or those containing inorganic components. Raman spectroscopy is the one of the few analytical techniques which can positively identify and characterize both elements and molecules. Raman spectroscopy can unambiguously identify

both the purity and physical form of elemental carbon, germanium, sulphur and silicon, the last mentioned being very important in the semiconductor industry as described in Sections 6.6 and 6.9. Raman spectroscopy is the only analytical technique which can positively identify and characterize elemental carbon from the shape and position of the bands in the spectrum. Starting with amorphous carbon, the bands sharpen as the crystallinity increases and then reach the ultimate with pure diamond giving a single sharp band at  $1365\text{ cm}^{-1}$ . However the ability to carry out this examination is dependent on the exciting wavelength. The spectrum of diamond can easily be recorded at  $1064\text{ nm}$  excitation (Figure 6.1) but amorphous carbon usually causes strong absorption and burning.

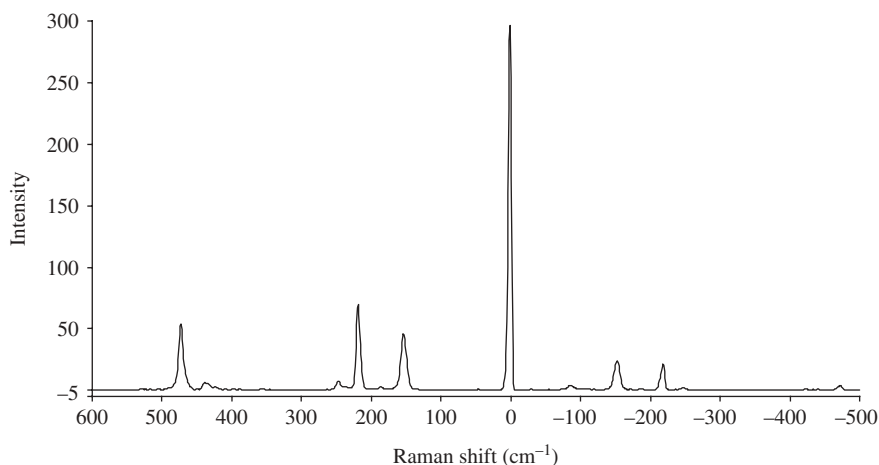
Spectra of amorphous carbon and graphite have been readily recorded with visible excitation [1, 2], but they can be recorded at  $1064\text{ nm}$  only by employing dilution techniques. Elemental sulphur is another strong Raman absorber with strong bands at  $\sim 200\text{ cm}^{-1}$ . It is sometimes used as a standard for instrument performance checks. The spectra do however vary with physical form. Flowers of sulphur (monoclinic) have a different spectrum from other sulphur forms [3]. Figure 6.2 shows both Stokes and anti-Stokes bands of sulphur.

Early work carried out in Raman spectroscopy showed its strength with inorganics. Particulates in urban dust [4] such as anhydrite, calcite, dolomite and quartz have been identified and characterized. Early microprobes [5, 6] were used to record the spectra of gaseous, liquid and solid inclusions in minerals. These include  $\text{CH}_4/\text{CO}_2/\text{N}_2$  ratios and solids such as apatite, calcite, nacholite and sulphur [7]. Inorganics have also been identified in biological samples, e.g. copper sulphide needles inside the lysosomes of *Littorina littorea* [8].

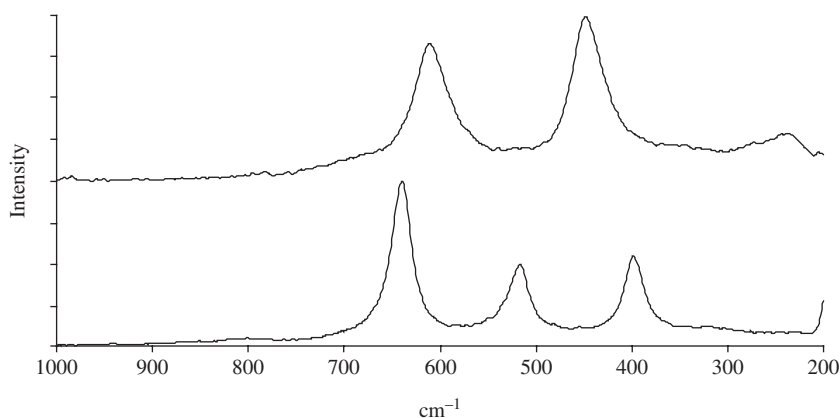
Figure 6.3 quite clearly shows the differences in the Raman spectra of the rutile and anatase forms of titanium dioxide, an important industrial filler for



**Figure 6.1.** NIR FT Raman spectrum of diamond.



**Figure 6.2.** NIR FT Raman spectrum of sulphur showing both Stokes and anti-Stokes shifts.



**Figure 6.3.** NIR FT Raman spectra of TiO<sub>2</sub> – rutile (top); anatase (bottom).

polymers. This difference has been employed quantitatively for plant control as described in Section 6.9. The breadth of the TiO<sub>2</sub> bands is quite unusual for the Raman spectrum of an inorganic compound. The vast majority of inorganic compounds have spectra with very sharp bands. The sharp bands make them relatively easy to pick out in the spectra of other compounds. In many cases the Raman spectra of organic materials have strong bands in the same position as in the infrared spectrum; with inorganic materials there are some notable exceptions. In the spectra of sulphates the bands have very different shapes but are in similar positions in the spectrum, whilst the carbonate bands are

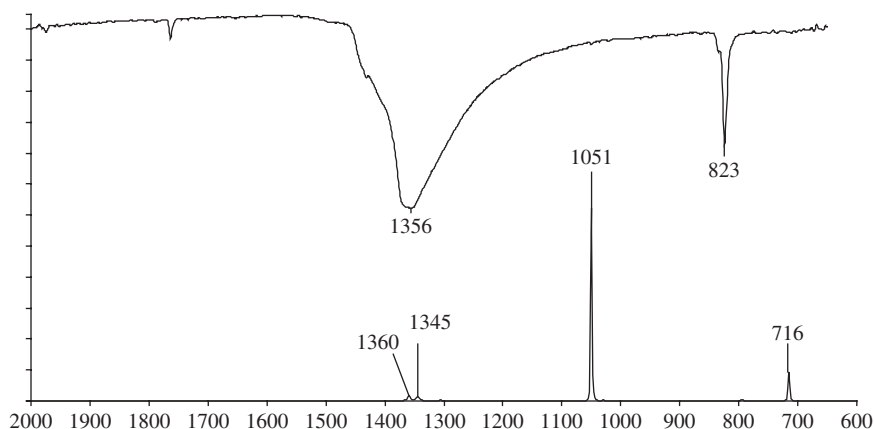


significantly moved (Figure 6.4). This is due to the relative intensities of symmetrical and asymmetrical vibrations.

A list of band positions observed in some common inorganic compounds is given in Table 6.1. The spectra were recorded with a 1064 nm exciting wavelength. Copies of the spectra, in PDF format, are available on the Internet [9]. This is one of the few application areas where there are published texts [10, 11] on a collection of specific Raman band positions. Using other exciting wavelengths generally does not affect the band positions but there are apparent exceptions [12]. Besides the normal background fluorescence, specific bands in minerals have been reported due to fluorescence. These can be misinterpreted as chemical group bands. Features to be aware of in studying the Raman spectra of inorganic materials are the changes which can occur due to the form or orientation of the crystal in the beam. Inorganic compounds tend to be more crystalline than many organic compounds and hence more susceptible to these effects. As discussed in Chapter 2 particle size effects can also change the spectrum.

Minerals are naturally occurring inorganic molecules with specific structure and form. As stated previously, a lot of early Raman spectroscopy and microprobe work was carried out on minerals, the latter for the identification of impurities and inclusions [13]. This area has found geological applications in studying both terrestrial [14] and extra-terrestrial [15] materials. Again, tables of known band positions have been published for minerals [16].

There has been a slow but growing increase in the use of Raman spectroscopy for commercial applications of both inorganic and mineral analysis:  $\text{TiO}_2$  plant monitoring, which has already been mentioned, quantitative methods for inorganics in storage tanks [17], diamond quality checks [18, 19] and testing of various jade minerals [20].



**Figure 6.4.** Infrared and NIR FT Raman spectra of  $\text{NaCO}_3$ .

**Table 6.1.** List of band positions in  $\text{cm}^{-1}$  observed in some common inorganic compounds. Bold type indicates the strongest bands

Ammonium	Carbamate	<b>1039</b>				
Diamond	Carbon	<b>1331</b>				
Ammonium	Carbonate	<b>1044</b>				
Calcium	Carbonate	<b>1087</b>	713	282		
Lead (II)	Carbonate	1479	1365	<b>1055</b>		
Potassium	Carbonate	<b>3098</b>	1062			
Strontium	Carbonate	<b>1072</b>				
Potassium	Carbonate (99.995%)	<b>1062</b>	687			
Potassium	Carbonate (99.995%), rotator	<b>1061</b>	686			
Sodium	Carbonate (anhydrous)	<b>1069</b>				
Sodium	Carbonate (anhydrous), rotator	<b>1080</b>	701			
Sodium	Carbonate AR	1607	<b>1080</b>	1062		
Sodium	Carbonate monohydrate	<b>1070</b>				
Potassium	Carbonate (99.995%), rotator	<b>1061</b>				
Potassium	Carbonate, Aldrich, 99%	<b>3098</b>	1062			
Sodium	Chloramine-T, sodium salt	3069	2921	1600	1379	1213
Sodium	Dichloroisocyanurate	1733	1051	707	577	<b>1132</b>
Potassium	Dichromate	<b>909</b>	571	387	235	230
Sodium	Dichromate ( $2\text{H}_2\text{O}$ )	<b>908</b>	371	236		
Potassium	Dichromate, rotator	<b>909</b>	570	374	235	
Potassium	Dichromate, rotator	<b>909</b>	570	374	235	
Ammonium	Dihydrogen orthophosphate	<b>925</b>				
Ammonium	Dihydrogen orthophosphate	<b>923</b>				
Potassium	Dihydrogen orthophosphate	<b>915</b>				
Titanium	Dioxide (anatase)	<b>639</b>	516	398		
Titanium	Dioxide (rutile)	610	<b>448</b>	237		
Sodium	Dithionite	1033	364	<b>258</b>		
Sodium	Dithionite	1033	364	<b>258</b>		
Ammonium	Ferrous sulphate ( $6\text{H}_2\text{O}$ ), rotator	<b>982</b>	613	453		
Sodium	Hexametaphosphate	<b>1162</b>				
Ammonium	Hydrogen carbonate	<b>1045</b>				

**Table 6.1.** Continued

Caesium	Hydrogen carbonate	<b>1012</b>	671	634		
Potassium	Hydrogen carbonate	1281	<b>1030</b>	677	193	
Sodium	Hydrogen carbonate	1269	<b>1046</b>	686		
Di-ammonium	Hydrogen orthophosphate	<b>948</b>				
Di-ammonium	Hydrogen orthophosphate	<b>948</b>				
Di-sodium	Hydrogen orthophosphate	1131	1065	<b>934</b>	560	
Di-potassium	Hydrogen orthophosphate (trihydrate)	1048	<b>950</b>	879	556	
Potassium	Hydrogen sulphate	1101	<b>1027</b>	855	581	327
Sodium	Hydrogen sulphate	<b>1065</b>	1004	868	601	
Sodium	Hydrogen sulphate (monohydrate)	<b>1039</b>	857	603	412	
Calcium	Hydroxide	1086	<b>358</b>			
Sodium	Hydroxide	<b>205</b>				
Lithium	Hydroxide (monohydrate)	1090	839	517	397	<b>213</b>
Ammonium	Hydroxy chloride	1495	<b>1001</b>			
Potassium	Iodate	<b>754</b>				
Sodium	Metabisulphite	<b>1064</b>	660	433	275	
Barium	Nitrate	<b>1048</b>	733			
Bismuth	Nitrate	<b>1037</b>				
Lanthanum	Nitrate	<b>1046</b>	739			
Lithium	Nitrate	<b>1384</b>	<b>1070</b>	735	237	
Potassium	Nitrate	<b>1051</b>	716			
Silver	Nitrate	<b>1046</b>				
Sodium	Nitrate	1386	<b>1068</b>	725	193	
Magnesium	Nitrate (6H <sub>2</sub> O)	<b>1060</b>				
Iron(III)	Nitrate (9H <sub>2</sub> O)	<b>1046</b>				
Potassium	Nitrite	1322	<b>806</b>			
Silver	Nitrite	<b>1045</b>				
Sodium	Nitrite	<b>1327</b>	828			
Sodium	Nitrite	<b>1327</b>	828			
Silver	Nitrite, rotator	<b>1045</b>	847			
Sodium	Nitroprusside (2H <sub>2</sub> O)	2174	1946	1068	656	<b>471</b>

Tri-potassium	Orthophosphate	<b>1062</b>	940			
Tri-sodium	Orthophosphate	<b>941</b>	415			
Tri-sodium	Orthophosphate	1005	<b>940</b>	548	417	
Tri-potassium	Orthophosphate	<b>1062</b>	<b>972</b>	857	549	
Tri-sodium	Orthophosphate (12H <sub>2</sub> O)	<b>939</b>	407			
Tri-sodium	Orthophosphate (12H <sub>2</sub> O)	<b>940</b>	550	413		
Tri-potassium	Orthophosphate (H <sub>2</sub> O)	<b>1061</b>	939			
Tri-potassium	Orthophosphate (H <sub>2</sub> O), rotator	<b>1061</b>	940			
Cupric	Oxide	<b>296</b>				
Zinc	Oxide	<b>438</b>				
Cupric	Oxide, rotator	<b>297</b>				
Zinc	Oxide, rotator	<b>439</b>				
Magnesium	Perchlorate	<b>964</b>	643	456		
Ammonium	Persulphate	<b>1072</b>	805			
Potassium	Persulphate	1292	<b>1082</b>	814		
Sodium	Persulphate	1294	<b>1089</b>	853		
Sodium	Phosphate	<b>938</b>				
Calcium	Silicate	<b>983</b>	578	373		
Lithium	Silicate	<b>601</b>				
Zirconium	Silicate	3019	<b>2821</b>	2662	1004	197
Lithium	Silicate					
Calcium	Silicate hydrous, commercial	<b>589</b>	578	372		
Magnesium	Rotator	677	<b>195</b>			
Magnesium	Silicate hydrous (talc)	676	<b>194</b>			
Magnesium	Silicate hydrous (talc), rotator	677	362	<b>195</b>		
Aluminium	Silicate hydroxide (kaolin)	<b>466</b>				
Aluminium	Silicate hydroxide (kaolin), rotator	912	791	752	705	276
Ammonium	Sulphate	<b>975</b>			430	338
Barium	Sulphate	<b>988</b>	454			
Barium	Sulphate	<b>988</b>	462			
Calcium	Sulphate	1129	<b>1017</b>	676	609	500
Magnesium	Sulphate	<b>984</b>				
Potassium	Sulphate	1146	<b>984</b>	618	453	

Table 6.1. Continued

Silver	Sulphate	969					
Sodium	Sulphate (anhydrous)	993					
Calcium	Sulphate (dihydrate)	1135					
Zinc	Sulphate (heptahydrate)	985	1009	669	629	491	415
Barium	Sulphate, Raman microscope	986	458				
Barium	Sulphate, rotator	988	462				
Barium	Sulphate, static	988	462				
Sodium	Sulphite	987	950	639	497		
Potassium	Sulphite	988	627	482			
Magnesium	Thiosulphate (hexahydrate)	1165	1000	659	439		
Sulphur	–	471	216	151			
Barium	Thiosulphate	1004	687	466	354		
Potassium	Thiosulphate (hydrate)	1164	1000	667	446	347	
Sodium	Thiosulphate (pentahydrate)	1018	434				
Potassium	Titanium oxalate	1751	1386	1252	850	530	300
Potassium	Titanium oxalate (2H <sub>2</sub> O)	1751	1384	1253	851	526	299

### 6.3 ART AND ARCHAEOLOGY

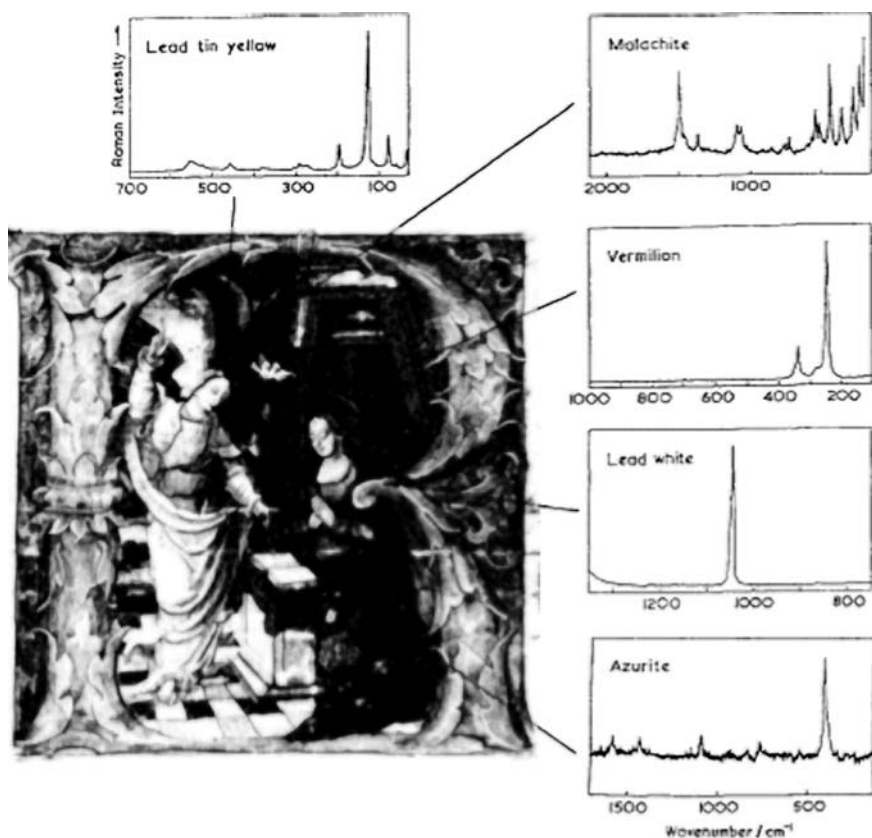
One of the major advantages of Raman spectroscopy in this field comes from the difficulties of obtaining samples for analysis. The materials to be examined are either very valuable in themselves or part of an object which is extremely valuable. Removing even the smallest sample for analysis would cause damage and subsequent loss of value. Raman spectra can be obtained from microsamples or by use of confocal techniques from under layers without having to separate them. When even microsamples cannot be taken, then examination can take place using sensing heads at the end of fibre optic probes and/or by remote sensing [21]. There is extensive knowledge of the compositions of colour used in paintings and decorated *objects d'art*. For many centuries colouring came from inorganic pigments and natural dyes. There were very few synthetic dyes available until the 19th century. Raman spectroscopy can not only identify the type of inorganic materials used but also the physical forms. The use of the dyes, pigments and resins [22] can be established chronologically [23]. By examining the Raman spectra of paintings [24] and archaeological artefacts such as pottery [25] the age of the work can be determined. Figure 6.5 demonstrates this feature very well. The knowledge of the composition can be used to distinguish original work from restoration and/or forgery.

Besides colour identification, the identification of gemstones [26], porcelains [27], metal corrosion products [28] and organic materials such as resins [29] and ivory [30] makes Raman spectroscopy a very valuable technique in this field. Ivory, of particular interest, has been studied for environmental purposes and by law enforcement bodies. Vibrational spectroscopic assignments of mammalian ivories have been published [31].

### 6.4 POLYMERS AND EMULSIONS

#### 6.4.1 Overview

The applications of Raman spectroscopy to polymers are extensively reported in the literature. A recent publication [32] devoted 10 chapters to the vibrational analysis of polymers with Raman spectroscopy being extensively used. Only a general overview is given here in an attempt to highlight some of the strengths. Polymers have been studied for identification, structure, composition, cure and degree of polymerization in the solid, melt, film and emulsion states. Ironically, polymers, particularly aliphatic ones, are not very strong Raman scatterers and sample preparation techniques such as folding thin films have to be employed. Conversely items such as aspirin can be studied, by Raman spectroscopy, inside a film wrap without interference from the film. In the early days Raman studies of polymers were restricted by fluorescence and thermal absorption due to



**Figure 6.5.** Sixteenth-century German choir book: historiated letter 'R'. (Reproduced with permission from R.J.H. Clark, *Journal of Molecular Structure*, **347**, 417–428 (1995).)

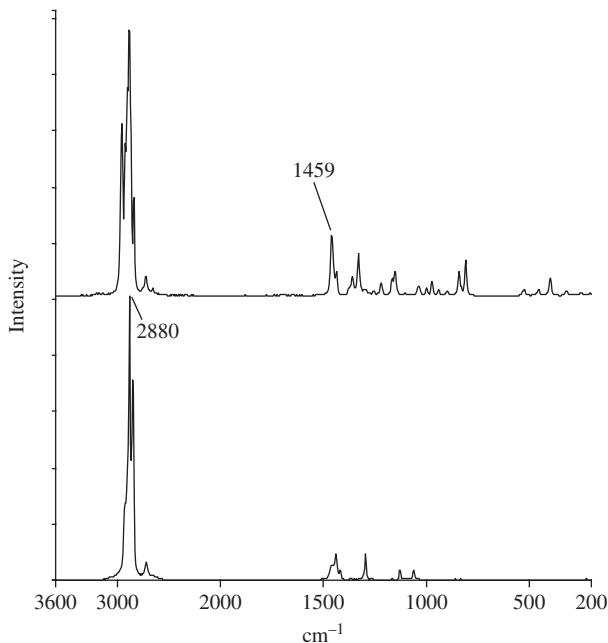
impurities and fillers. These have been largely overcome by NIR visible, UV dispersive excitation and 1064 nm FT excitation. Cleaner processes leading to fewer residues have also helped. However some commercial products still contain anti-oxidants, plasticizers and fillers which can cause interferences. Both the chemical and the physical nature of the polymers themselves have to be considered before examination by Raman spectroscopy. Whilst Raman spectroscopy can be considered a minimal sample preparation technique, the physical state (granules, film, etc.), the morphology (macro- and micro-crystallinity), thermal properties (high/low melting), state of cure, copolymer distribution and homogeneity of fillers can all affect the way in which a sample is presented to the Raman spectrometer. Many samples can be placed directly in the beam for 90° or 180° signal collection. Samples can be presented in glass bottles and aqueous emulsions can be studied. However, for the latter 'particle' size relative

to the exciting wavelength needs to be considered. Care has to be taken if, in order to detect weak scatters the laser power is increased. This may cause thermal damage or induce changes.

### 6.4.2 Simple Qualitative Polymer Studies

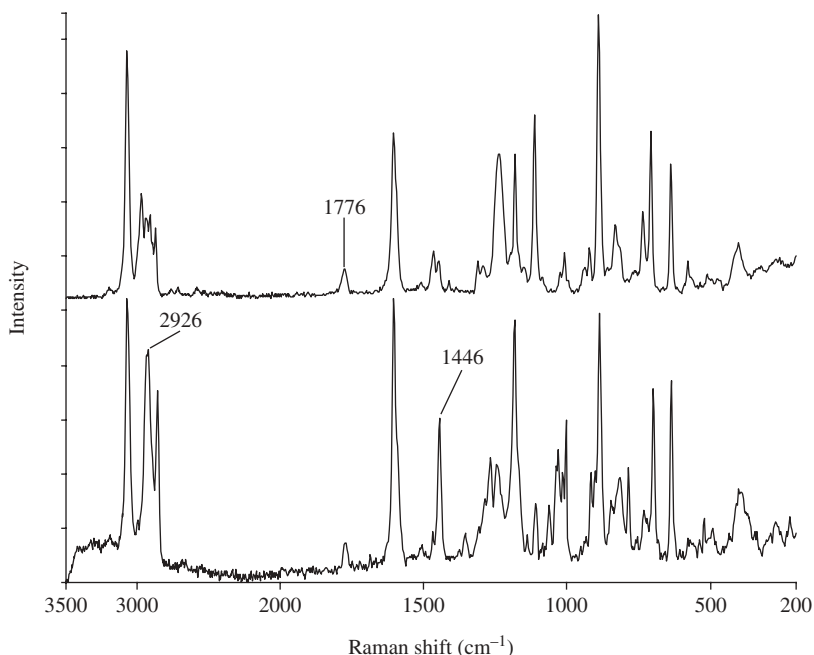
Of the many in-depth and wide ranging reviews written on Raman spectroscopy of polymers, a few relatively simple applications are described here to illustrate the range of the technique.

Whilst collections of Raman spectra are not common, a published collection of spectra of common polymers is available [33, 34]. The spectra of five of the most commonly encountered polymers, polyethylene (PE), polypropylene (PP), polyethylene terephthalate (PET), polycarbonate and polystyrene were all recorded quickly and easily on an FT Raman spectrometer with no sample preparation. In Figure 6.6 the spectra are quite distinctive even to subtleties of chain branching between PE and PP in the 2900 and 1450  $\text{cm}^{-1}$  region of the spectrum. Figure 6.7 shows that whilst the polycarbonate spectra are dominated by the bands due to the aromatic groups, differences between the aliphatic methyl and cyclohexyl groups are quite clear. The bands are in the same



**Figure 6.6.** NIR FT Raman spectra of polypropylene (top); polyethylene (bottom).

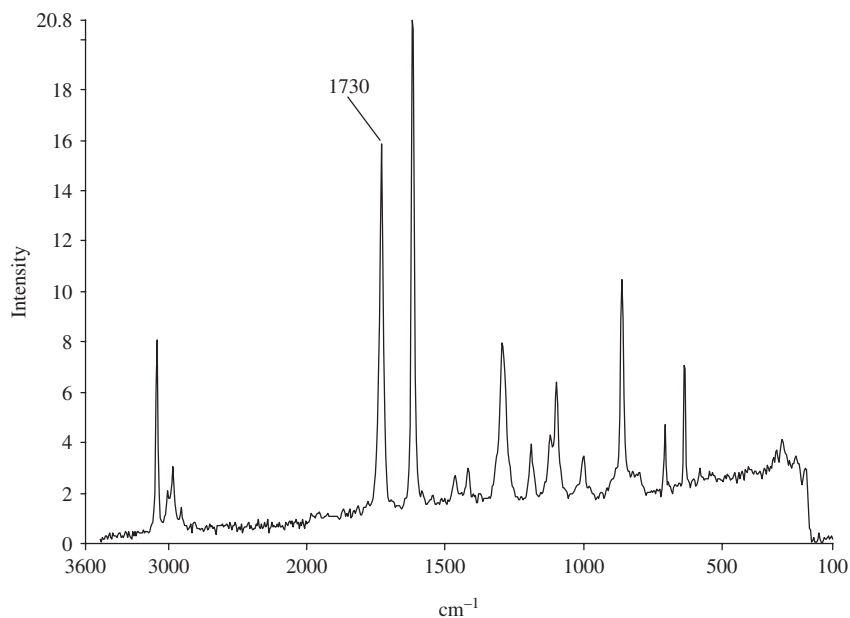




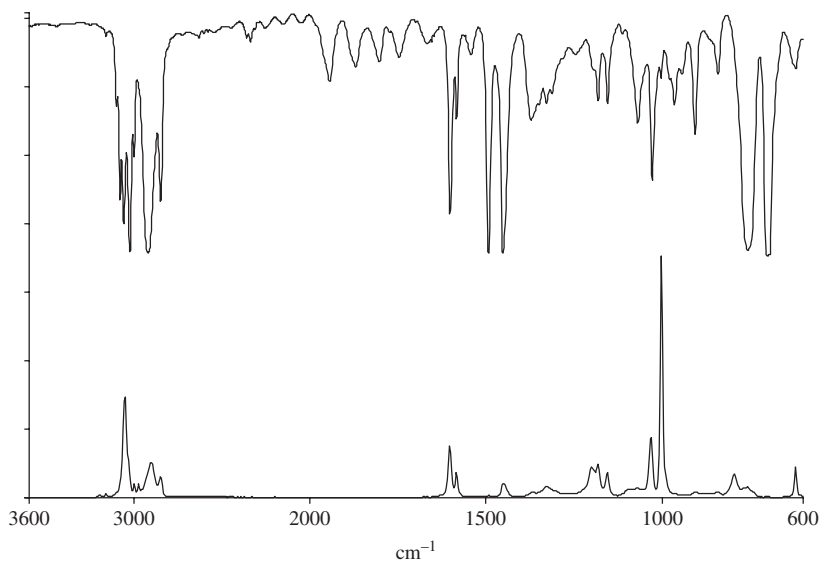
**Figure 6.7.** NIR FT Raman spectra of two polycarbonates.

spectral regions as in the PE and PP spectra shown in (Figure 6.6). The spectrum of PET, also shows a strong band due to the carbonyl group (Figure 6.8). This quite distinctive spectrum is also presented in Section 6.5 where the PET is seen as part of a matrix. These spectra also give the lie to the often perpetrated myth that asymmetric groups such as carbonyls do not appear in Raman spectra. The band at  $1776\text{ cm}^{-1}$  in Figure 6.7 is due to the carbonyl stretch. In Figure 6.9 the comparison of infrared and Raman spectra of polystyrene does show how Raman spectra emphasizes the bands from aromatic groups. Because of the ability to show these sometimes subtle differences, Raman spectroscopy has been used to create microscopic images of the distribution of polymers in blends [35]. Differences in morphology, polymer chain ordering and molecular orientation have been the subject of in-depth studies [36–41]. One of the most effective combinations is to employ both infrared and Raman imaging techniques to study these features [42].

In addition to the study of the polymers themselves, Raman spectroscopy has been used to study polymer composites. These often have other components added for strength or to preserve the lifetime by reducing oxidation or free radical attack. The fillers are often inorganics such as silicates, carbonates and elemental carbon or sulphur. The Raman spectra of these, as seen earlier, are



**Figure 6.8.** NIR FT Raman spectrum of PET.

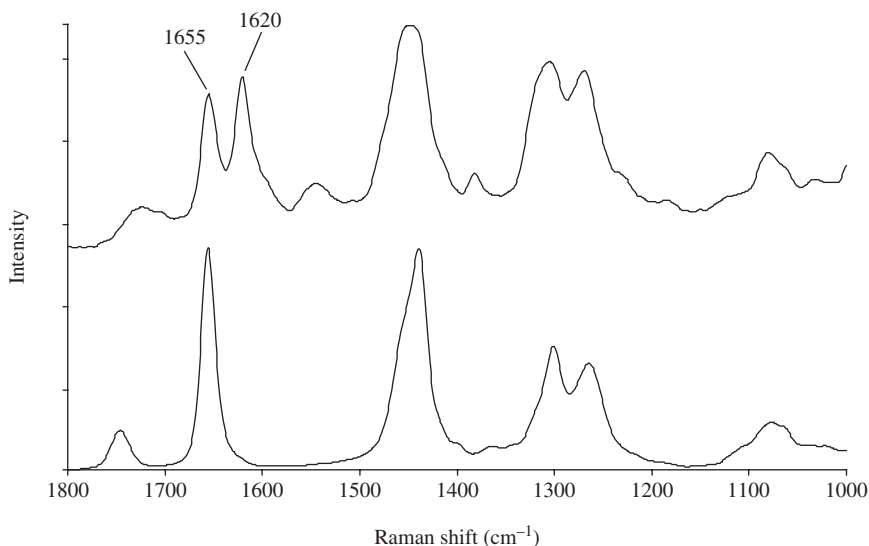


**Figure 6.9.** Spectra of polystyrene – infrared transmission spectrum (top); FT Raman (bottom).

quite distinctive. The variation in spectra can give information on the chemical and physical composition [43] and strength of the composite.

Raman spectra can identify the type of polymer present in a material but can also be used to study how far polymerization has occurred [44, 45] or even how far a polymer has been degraded [46, 47]. The double bond in acrylates is very strong and quite characteristic. As polymerization occurs the strength of this bond decreases. This can be easily monitored by Raman spectroscopy and has been developed for a number of applications for plant scale monitoring. Acrylate-based emulsions are quite common. In another example, the variation in the band due to  $>C=C<$  at  $1655\text{ cm}^{-1}$  can be seen in Figure 6.10 for sunflower oil. The top spectrum is an emulsion with degraded sunflower oil. The bottom is a Raman spectrum of the pure oil.

Following the polymerization of dispersions of polymer in aqueous media is very difficult by conventional methods. However, by using a fibre optic probe, following the reduction of a band from the monomer by Raman scattering is quite feasible, in glass vessels under manufacturing conditions. Whilst this experiment is relatively easy to carry out in principle, one must consider the relative size of the emulsion drops in the suspension and the laser wavelength employed. This is similar to the particle size effects discussed in Chapter 2. The opposite of following a polymerization reaction is to monitor degradation of a polymer. One of the earliest reported degradation studies [48] was on polyvinyl chloride (PVC). As PVC degrades, hydrogen chloride (HCl) is lost and conjugated double bonds form. The wavenumber position in the Raman



**Figure 6.10.** NIR FT Raman spectra of oils – emulsion (top); pure oil (bottom).

spectrum shows the number of bonds in a chain which have been formed and hence the degree of conjugation and degradation. The studies by Gerrard and Maddams showed intense bands at 1511 and 1124  $\text{cm}^{-1}$  associated with conjugation unsaturation. By variation of the illuminating laser line they showed that the intensity was due to resonance effects. They also showed that the position of the band due to  $>\text{C}=\text{C}<$  between 1650 and 1500  $\text{cm}^{-1}$  correlated with the length of the sequence. Subsequent workers [48–51] have used these bands to study similar sequences in various polymers.

### 6.4.3 Quantitative Polymer Studies

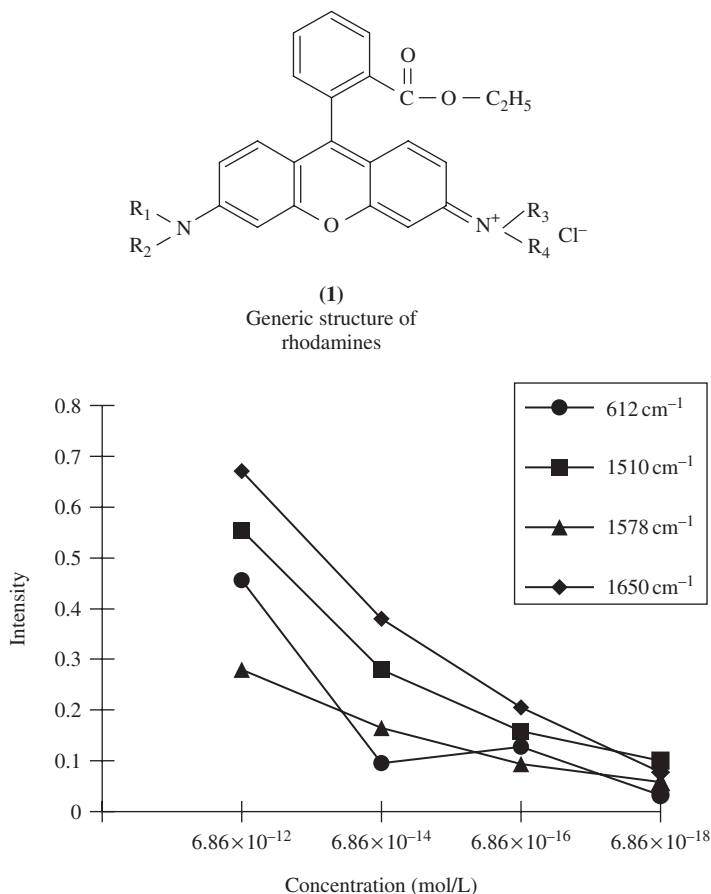
The applications described have largely dealt with the physical and chemical characterization of polymers. In several of the cases cited, quantitative aspects can also be measured. Quantitative measurements in Raman spectroscopy of polymers vary from the relatively simple to the quite complex. The relative intensities within a normal Raman spectrum will simplistically be directly proportional to concentrations of the species present, the laser power and the Raman scattering cross-section. As the scattering cross-section is very difficult to determine, absolute band strengths are rarely, if ever, determined. Determination of relative strengths by using band ratios is most common. This method can easily be employed in the examples already cited of PVC degradation, degrees of polymerization of acrylics and epoxides, and filler content. More complex studies often have to employ more sophisticated quantitative techniques which involve several bands or complete regions of the spectrum. These can employ principal component analysis (PCA), factor analysis (FA), principal component regression (PCR) and partial least squares (PLS). This is particularly the case where multi-component blends, composites or morphological features are being studied. An example of this is the modelling of PET density from normalized, mean-centred FT Raman spectroscopy studies. The bandwidth of the carbonyl band in the Raman spectrum has been associated with the density and hence the sample crystallinity [52].

## 6.5 COLOUR

### 6.5.1 Raman Colour Probes

Raman spectroscopy is very sensitive to coloured molecules. Indeed using visible laser sources highly coloured materials can exhibit too much sensitivity and be the cause of many difficulties. Coloured molecules can be so strongly absorbing as to thermally degrade. There are ways of diminishing this effect by spinning samples or diluting them in a matrix such as hydrocarbon oil or potassium bromide (KBr) powder. Moving to a higher wavelength source can mitigate this effect but even

small amounts of some colours can still cause problems. A combination of two Raman techniques, described in Chapter 5, can both overcome the fluorescence effects and show large increases. Surface enhanced Raman spectroscopy (SERS) gives a  $10^6$  increase in sensitivity and also strongly quenches fluorescence. Resonance Raman spectroscopy (RR) gives a  $10^4$  increase. The combination of the two techniques, surface enhanced resonance Raman spectroscopy (SERRS), gives a  $\sim 10^{10}$  enhancement. Early SERRS studies of rhodamines 3G, 6G (Figure 6.11) and 3B (**1**) have detected the dye in solution at  $\sim 10^{-10}$  mol but more recent studies have claimed detection limits of  $\sim 10^{-18}$  mol which is roughly equivalent to having 35 molecules in the beam at a given time [53–56].



**Figure 6.11.** Graphical representation of intensity vs. concentration for four peaks selected from the R 6G SERRS spectra using nitric acid aggregation (points corresponding to R 6G concentration of  $6.8 \times 10^{-10}$  M were omitted). (Reproduced with permission from C. Rodger, W.E. Smith, G. Dent and M. Edmondson, *J. Chem. Soc. Dalton.*, 791 (1996).)

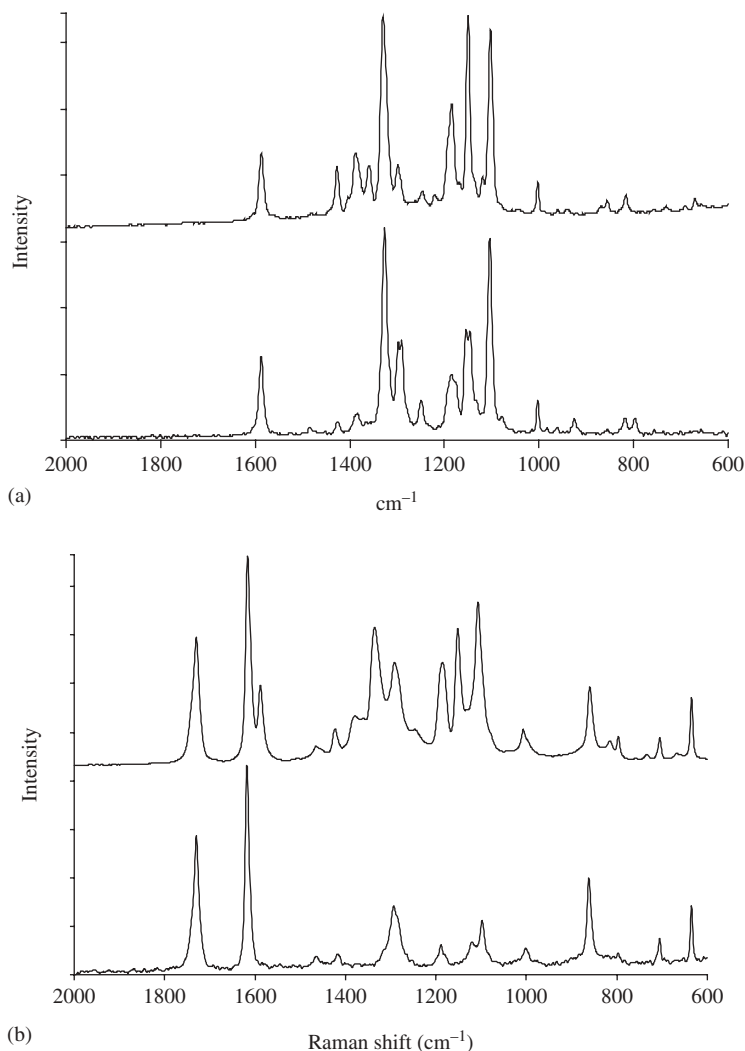
The experiment can be carried out in a laboratory only in the absence of a dye laser spectrometer as this is a potential source of contamination at these levels. This low level of detection limit has opened up the field of SERRS probes to otherwise prohibitive areas of vibrational spectroscopy. This is particularly true in the biological area. In many cases the applications are outside the scope of vibrational spectroscopy. Infrared spectroscopy is limited by the strong absorption of water. Conversely, Raman spectroscopy can cope with aqueous media and the applications are expanding. One area of much interest is tagging DNA with a chromophore rather than with a fluorophore (see Section 5.7). By employing SERRS techniques which are very sensitive and specific to the chromophore, levels of DNA at  $10^{-15}$  molar have been detected [57–59].

### 6.5.2 *In Situ* Analysis

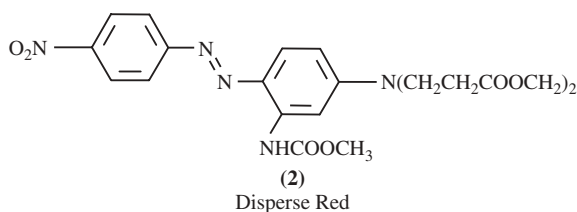
The major advantage of Raman spectroscopy in the application of colour probes is that vibrational spectroscopy can be used as a largely non-destructive, *in situ* sampling technique. Dyes and pigments can have the spectra recorded as neat samples inside vials and bottles with no concern for sample preparation changing the form. The same dyes and pigments can now be studied while in use in the applications for which they were designed. The strength of Raman signals from coloured molecules has already been discussed. However when the dye and pigments are used to colour materials, the amount of dye is relatively low, e.g. a 2% dye loading on a polymer, can still be detected by Raman spectroscopy [60]. The low concentration has the effect of diluting the colour and reducing thermal degradation, similar to the mull and halide disk techniques. This enables strong Raman spectra to be recorded where the bands due to the colour component can predominate. The strong bands which appear in the Raman spectrum are from the part of the molecule generating the chromophore and weak bands appear from the rest of the molecule. The reason for these extra-strong bands with visible laser sources is quite often attributed to resonance. This does not explain why a similar chromophore enhancement is sometimes observed with 1064 nm laser sources on dyes with only weak absorptions in this region. The likelihood is that enhancement is due to pre-resonance [61] (see Section 4.2.2). This feature can be used to study changes in dye conformers and the effect or otherwise on the chromophore part of the molecule not only on the neat dye but also that dispersed in the material being dyed. A disperse red dye (**2**) for polymer textiles has been shown to exhibit more than one physical form by liquid and solid NMR studies [62, 63]. NIR FT Raman spectra of the solid samples of the dye showed differences in the azo band positions and also in the backbone structure of the molecules. A piece of poly(ethylene terephthalate) ester cloth dyed at ~2% level with disperse red

was examined directly in the spectrometer beam at 1064 nm excitation. The spectra of forms I and II are shown in Figure 6.12a. The dyed cloth and undyed cloth are shown in Figure 6.12b.

The bottom spectrum of Figure 6.12b whilst showing strong bands due to the poly(ethylene terephthalate) fibres also shows bands due to the dye. It is clear

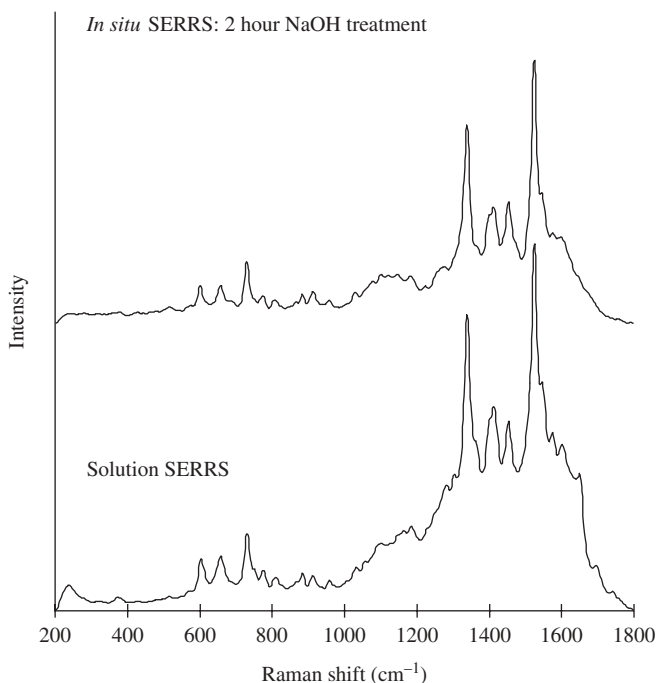


**Figure 6.12.** NIR FT Raman spectra of (a) azo dye, forms I (top) and II (foot); (b) red cloth – dyed (top); PET (bottom).



from this spectrum that form I of the dye is predominant whilst the dye is in the fibre.

The resonance effect of the chromophore can be enhanced by use of the SERRS technique. It also enables *in situ* identification of chromophores from small samples. This technique has been used to identify chromophores in pen inks [64], dyed fibres [65] and lipsticks [66]. With polymer fibres the dyes are dispersed in the fibre but with cellulose the dyes can be reacted onto the fibre. The SERRS technique has been used to detect dyes at very low levels reacted onto the fibre [68] as shown in Figure 6.13. The lower spectrum shows the dye



**Figure 6.13.** SERRS spectra of reactive dye attached to a cellulose fibre and in solution. (Reproduced from reference [68] by kind permission of Dr C. Rodger.)

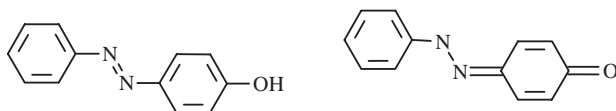


in solution. The upper spectrum is of the dye attached to a fibre which had been treated in caustic solution for 2 h. This was to ensure that the dye was firmly attached and would not leech back into the SERRS colloid.

Dyes and pigments are used for printing in a number of different printing mechanisms and applications [67]. One of the fastest growing areas for the use of dyes is in the ink of inkjet printers. The dyes first developed for these inks were very similar to those used for textiles. The requirements of the ink manufacturers were very different from the textile dyers. Only three main colours, cyan, yellow and magenta were required. The dyes had to have high colour, with good light and wet fastness. Unlike textiles the dyes could not be fixed to the paper by boiling! Dye development occurred along the non-chromophoric part of the dye to increase fastness to the inkjet media. Originally, the inkjet medium was cellulose paper of varying complex composition and pH, but now it can be polymers, gels, textiles or electronic surfaces. Studies of the behaviour of the dyes on various types of paper surfaces to determine the effects on the chromophore of pH have been carried out [68, 69]. By using both SERRS and NIR FT Raman techniques, the behaviour of the dyes can be studied as solids, on the surface of the paper and below the surface. The effect of varying the non-chromophoric constituents on the chromophore in various parts of the media under differing pH conditions can be studied in this way.

### 6.5.3 Raman Studies of Tautomerism in Azo Dyes

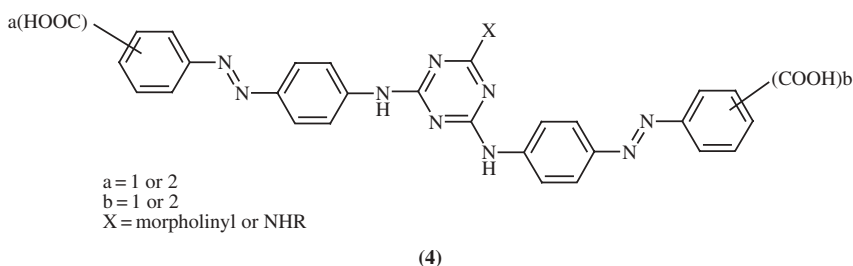
The changes seen in the *in situ* analysis of dyes can be due to physical or chemical form changes. Azo dyes are amongst the most extensively employed dyes in the colour industry. They are used for their electrical properties as well as their wide colour range. The azo group (3), which simplistically exhibits azo-hydrazo tautomerism, is symmetrical and therefore very weak in the infrared spectrum. The band can be strong in Raman spectra [70] at approximately  $1450\text{ cm}^{-1}$ . When the hydrazo is formed, the  $\text{--C=N--}$  band can be seen in the Raman spectrum at approximately  $1605\text{ cm}^{-1}$  with another strong band at  $\sim 1380\text{ cm}^{-1}$ , the origin of which is still not fully understood. Whilst this group is very important in colour chemistry, being a significant component in many dyes [71–73], the detection and interpretation of these bands can be complex and have been the subject of many studies by the authors.



(3)

Azo-hydrazo tautomers

A simple example of the comparative information obtained from the infrared and Raman spectra is a yellow diazo dye (**4**). The dye has a generic structure with azo, carboxyl and triazine groups. The upper infrared spectrum in Figure 6.14 is complex due to strong hydrogen bonding between groups. Bands at  $3500\text{--}2000\text{ cm}^{-1}$  show a mixture of salt and free carboxylic acid groups. The band at  $\sim 1550\text{ cm}^{-1}$  is probably due to the triazine ring. The general broadness is due to both the hydrogen bonding effects and the large size of the molecule. The azo groups cannot be seen in this infrared spectrum.

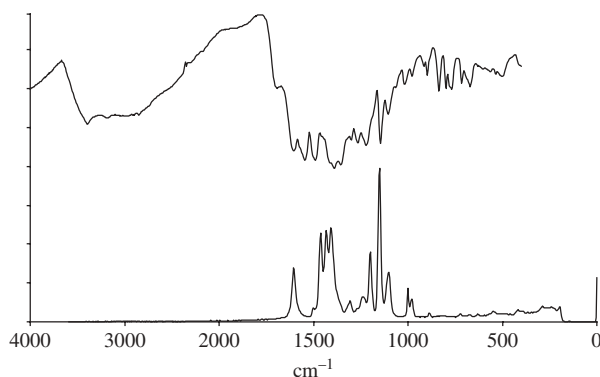


Generic structure of yellow diazo

Conversely, in the lower Raman spectrum the azo and aromatic bands dominate the spectrum, with the hydrogen bonded groups being too weak to observe.

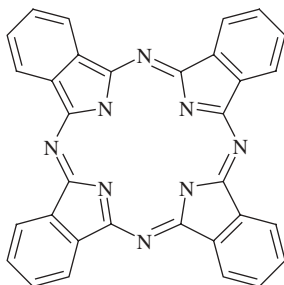
### 6.5.4 Polymorphism in Dyes

In the azo dyes, chemical group changes which could affect the colour properties were studied. Physical changes can also take place in the molecular structure



**Figure 6.14.** Infrared and NIR FT Raman spectrum of azo dye. (Reproduced with permission from J. Chalmers and P. Griffiths (eds), *Handbook of Vibrational Spectroscopy*, vol. 4, John Wiley & Sons, Inc., New York, 2001.)

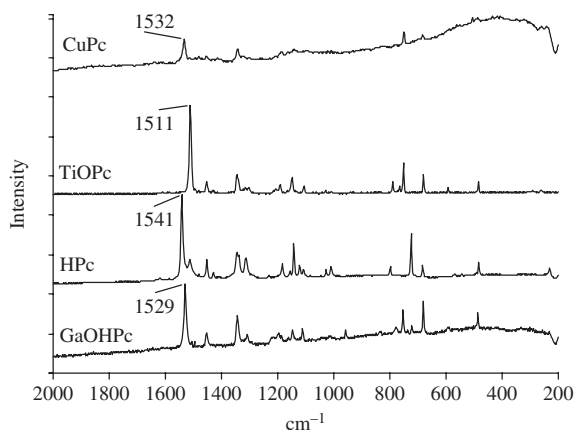
of a dye which in turn can also affect the properties. This effect is known as polymorphism, described in Section 6.7. In the electrophotography industry the electrical properties of organic materials can change the effectiveness of the device. In a photocopying machine or laser printer one stage of copying the image requires a charge to be generated in a photoreceptor which usually comprises several layers. The base is usually conducting, above which is a charge transfer generation (CTG) layer. On exposure to the laser an electronic hole is generated. This hole is transferred to the surface of the photoreceptor via charge transport material (CTM) in the charge transport layer. The wavelength of the illuminating laser is about 750 nm. The charge generating layer is less than 1  $\mu\text{m}$  thick to allow mobility and transfer of the generated hole. Dyes are often used to absorb energy at the irradiating laser wavelength and compose most of the CTG layer. The most adaptable dyes are the phthalocyanines. Their electrical properties vary with the metal co-ordinated in the ring. Metal-free phthalocyanine (**5**) also has interesting electrical properties. The position of the ring breathing band at  $\sim 1540\text{--}1510\text{ cm}^{-1}$  in the Raman spectrum is quite characteristic as can be seen in Figure 6.15.



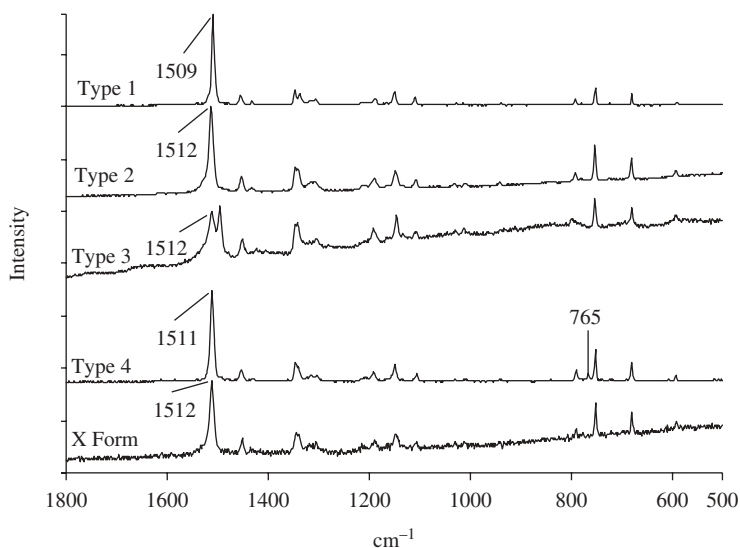
(5)

Metal-free phthalocyanine

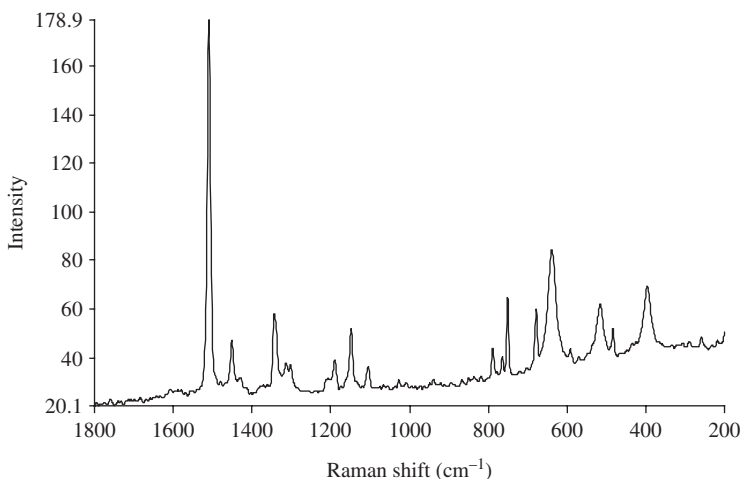
Titanium phthalocyanine (TiOPc) is most widely used. However, the speed of charge generation is vital. TiOPc has several polymorphs and only one is suitable for optimum charge generation. The Raman spectra of various TiOPc polymorphs in Figure 6.16 show subtle but distinctive changes. Type IV has a very small extra band at  $765\text{ cm}^{-1}$ . The spectrum of a drum placed directly in the beam of an NIR FT Raman spectrometer (Figure 6.17) shows this feature quite clearly. Bands are present from the other components – the covering polycarbonate layer, the CTM component and the base layer of titanium dioxide – but none have this band in their spectra. The confirmation of the correlation of this distinctive feature comes from the relative charge transfer speed of the devices with and without form IV.



**Figure 6.15.** NIR FT Raman spectra of various metal phthalocyanines. (Reproduced from NIR FT Raman examination phthalocyanines at 1064 nm, G. Dent and F. Farrell, *Spectrochim. Acta*, 1997, 53A, 1, 21 © 1997 by kind permission of Elsevier Science-NL, Sara Burgerhartstraat 25, 1055 KV Amsterdam, The Netherlands.)



**Figure 6.16.** NIR FT Raman spectra of the polymorphs of TiOPc. (Reproduced from NIR FT Raman examination phthalocyanines at 1064 nm, G. Dent and F. Farrell, *Spectrochim. Acta*, 1997, 53A, 1, 21 © 1997 by kind permission of Elsevier Science-NL, Sara Burgerhartstraat 25, 1055 KV Amsterdam, The Netherlands.)

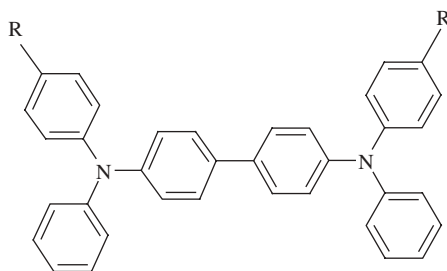


**Figure 6.17.** NIR FT Raman spectra of photocopier drum with anatase  $\text{TiO}_2$ . (J. Chalmers and P. Griffiths (eds), *Handbook of Vibrational Spectroscopy*, vol. 4, John Wiley & Sons, Inc., New York, 2001.)

In this application a coloured molecule has been used and studied by Raman spectroscopy because of the electronic properties. Studies of other materials used in the electronics industry have also been carried out.

## 6.6 ELECTRONICS APPLICATIONS

In the previous section the application of Raman spectroscopy to colour was generally concerned with the chemical and/or physical structure of the dye. However, colour can also be used effectively in electronic devices, for example to provide a detector or to produce an image. In electrophotography dyes, including phthalocyanine dyes were found to be very useful. The selectivity of resonance Raman scattering and the natural selectivity of Raman scattering make spectroscopy a good probe for these materials. As described in the previous section, when the charge generating drum is examined by Raman spectroscopy, bands are present from the phthalocyanine and from the other non-coloured components. These are the covering polycarbonate layer, the CTM component and the base layer of titanium dioxide. Information on all these components can be obtained. The titanium dioxide is clearly in the anatase form. The CTM composition tends to be based on triarylamines (**6**) with extra-strong aromatic bands due to the multiple conjugation. These materials transfer electrons under charge and are therefore strongly polarizable. The positions of these bands are very sensitive to the environment. These



(6)

Triarylamine

types of material besides being used in bulk, in copier and printer drums, are also being employed as very thin films or coatings in organic semiconductors such as field effect transistors [74–76], solar cells [77] and light emitting displays [78, 79]. The ability to carry out microscopic or *in situ* examination allows the study of these materials in the devices in which they are used. The types of materials employed in these devices are usually conducting polymers with conjugated  $\pi$ -electrons. Typical polymers initially employed were polyacetylene, poly(p-phenylenes), polythiophenes and poly(triarylamine)s [80–83]. Several of these have been available from commercial sources since 1996 [84]. Poly(p-phenylene vinylene)s (PVPPs) and spiro compounds have also been developed [85, 86]. A typical band gap of these polymers is 1–3 eV. A conjugated polymer can be doped with electron acceptors such as halogens, or donors such as alkali metals. The polymers can be discussed in concepts, new to the organic chemists, of solitons [87], polarons [88] and bipolarons [89]. Essentially the polymers carry charges or emitting light. As in other polymer applications the effectiveness of these materials is dependent on the morphology as well as the chemistry. However a further advantage is the change in the spectra that takes place in the excited state of the polymer. The electronic behaviour of the building block monomers, on which the polymers are based, can be studied by cyclic voltammetry (CV) to determine the oxidation and reduction points. This leads to Raman spectroelectrochemistry whereby the Raman spectra of the materials can be measured during the voltage cycle. This in turn leads to an understanding of the spectra generated in a device. Whilst this may appear to be a recent development, the original work which led to the discovery of the SERS effect by Fleischmann and Hendra [90] was of course an attempt to study electrochemical changes by Raman spectroscopy. Raman spectroelectrochemistry is discussed further in Section 7.1

Whilst electronically active polymers and organic semiconductors are at the forefront of technology, more conventional semiconductors have also been studied by Raman spectroscopy. Elements such as carbon, germanium and

silicon are widely used in the electronics industries for both their mechanical and electronic properties. As discussed in Section 6.9 this is probably one of the largest use for Raman spectroscopy as a quality control tool. Stress measurements have been discussed in polymers but can also be carried out in electronic devices, just as in polymers, shifts occur in the wavenumber position of the Si Raman bands. This shift can be used to obtain Raman maps of stress and crystallinity in silicon wafers [91, 92]. In heavily boron-doped silicon the LO (longitudinal optical) phonon line, which is a very sensitive Raman band, shifts to lower frequency and broadens as the boron concentration increases [93]. Films of fluorine-doped silicon dioxide have been monitored by Raman spectroscopy to determine the fluorine to oxygen ratios and hence the dielectric properties [94]. Silicon crystals are employed in ultra large-scale integrated (ULSI) circuits [95]. The Raman spectra of the crystals give information on the lattice modes and the behaviour of the crystals. The vibrations of crystals used in semiconductors are reflected in the behaviour of phonons. It is this behaviour which is studied by Raman spectroscopy. The structural characterization can include the crystallinity, crystallographic orientation, superlattices of mixed crystals, defects, and stacking faults. Besides the structural characterization, electronic characterization can be carried out. Both bound and free charges can contribute to Raman scattering, through collective and single-particle excitation processes. For those interested in studying the processes in greater depth than can be described here, there is the series 'Light Scattering in Solids I–VII' which appeared between 1982 and 2000 in *Topics in Applied Physics* published by Springer in Berlin. There are several other excellent review articles as well [96–99].

## 6.7 BIOLOGICAL AND PHARMACEUTICAL APPLICATIONS

### 6.7.1 Introduction

The biological and pharmaceutical areas of application lend themselves well to investigations by Raman spectroscopy. There are two particular aspects which are common to both areas. One is the possibility of studying materials *in situ*. In biological systems, wet live cells have been studied whilst in the pharmaceutical area tablets inside polymer containers have been identified. Another use of Raman spectroscopy is to study physical structure. In particular polymorphism is very important in the pharmaceuticals industry and there are a number of Raman studies. Similarly, in proteins and peptides, secondary structure has been studied at length, though in this case interpretation of the results can be quite complex. Some include more sophisticated techniques such as Raman optical activity (ROA) (see Chapter 7). This topic covers a very wide area of application on which specific chapters and books have been written. Indeed Chapters 4, 5 and 7 have a number of examples of Raman spectroscopy being

used very effectively for biological applications. In this section we can only give a flavour of the vast area of research and application. References and a bibliography will assist those with deeper interest.

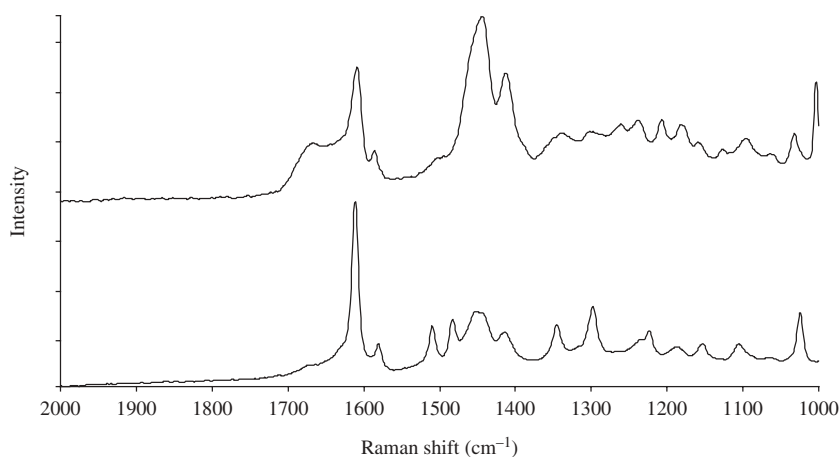
### 6.7.2 Biological Applications

Raman spectroscopy has advantages and disadvantages for the study of biological molecules. Amongst the advantages is the ability to study *in situ* aqueous systems. One of the disadvantages is that in using highly focussed beams, sensitive tissue is easily damaged. However there is a very wide range of biological systems which can be and have been studied by Raman spectroscopy [100]. As polar groups such as carbonyls, amines and amides are weak in the Raman spectrum, this would appear to be a disadvantage. However groups such as  $-S-S-$ ,  $-SH$ ,  $-CN$ ,  $-C=C-$  and aromatic rings give strong distinctive bands for specific characterization. Other groups such as carbonates and phosphates can also have distinctive Raman bands. The technique can also detect changes in physical form, so polymorphism, secondary structure in peptides and general molecular backbone changes can be detected. The use of  $180^\circ$  scattering with the development of microscopes and microprobes has led to automation for fast screening and the ability to examine systems *in situ*. In the case of microprobes, the enhancement techniques such as SERS and SERRS which can use metal colloids as part of the probe have brought large increases in sensitivity. The authors have used these techniques, as described in other sections, to detect DNA, and along with others are approaching single molecule detection. Among a vast number of applications reported are binding studies, genomics, lab on a chip, proteomics, protein interactions and solid phase synthesis. DNA and protein arrays as well as cell growth have been studied. There are also a large number of published studies in the food and biomedical fields. A few examples are: transitions in amino acid crystals [101], single-cell bacteria [102], bacterial spores [103], carotenoids in numerous systems including atlantic salmon [104], characterization of micro-organisms [105], fungi [106], grain composition [107], liposome complexes [108], yeast [109] and benign and malignant tissue in thyroid [110] and human breast tissues [111]. Specific studies of chromophore containing proteins can give good structural information from suspensions as illustrated for P450 enzymes in Section 4.4.2. Gradually, as equipment and skill improves through the work of some excellent groups, Raman scattering is becoming a useful technique in medicine, detecting *in situ* species such as pre-cancerous tissue and plaque.

### 6.7.3 Solid Phase Organic Synthesis/Combinatorial Chemistry

As mentioned in the previous section, one of the growing areas of interest for Raman spectroscopy is solid phase organic chemistry (SPOC) or combinatorial chemistry. Rather than being carried out in solution, reactions take place in/on

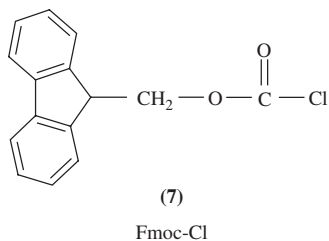




**Figure 6.18.** Spectrum of acrylate bead (bottom) and with peptide (top).

solid supports. These supports are usually beads of polyacrylate or polystyrene with reactive end groups such as hydroxyls, chlorine or glycol groups [112]. The beads are porous and have a cellular structure. The beads swell in the solvent and can become gelatinous. The reactants diffuse in and out of the beads with the reactions taking place at the active sites. Analysis of the beads is dependent on the information required (Figure 6.18). Often the phrase “on bead analysis” is used which leads to the erroneous conclusion that surface techniques apply. However, Raman spectroscopy can penetrate into the bead, enabling effective signals to be obtained. Approximately 90% of the reaction takes place in the bead. For research purposes single beads are often monitored but for more routine analysis batches of beads are usually studied. A recent comparison [113] of FTIR and FT Raman methods highlighted the strengths and weaknesses of both approaches. The advantages of Raman spectroscopy is once again the lack of sample preparation, weak absorptions from the solvents and the ability to carry out *in situ* studies. The beads themselves can be studied during preparation as reactive beads, or reactions taking place in/on the beads can be studied.

Peptide reactions can have several sequences of protection and de-protection. The 9-fluorenyl-methoxy-carbonyl (Fmoc) (7) strategy is an early developed system [114, 115].



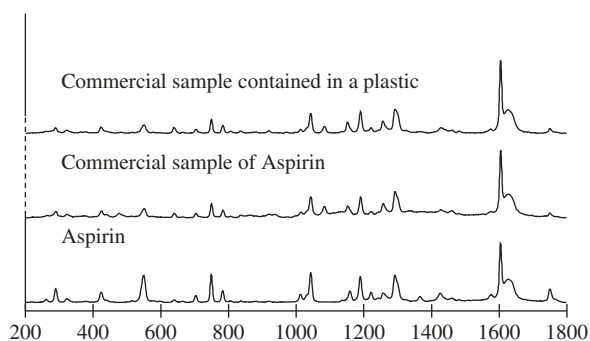
The stages have been monitored directly on the beads by investigating changes in the secondary structure [116]. The amide I and III bands were studied to gain information on the secondary structure of the growing peptide chain. Comparative studies of *in situ* reactions on beads have been carried out by FTIR and FT Raman spectroscopy [117–119]. More recently the use of dispersive Raman spectrometers has also been investigated for studies with flow through cells [120].

#### 6.7.4 Pharmaceuticals

The advantages of Raman spectroscopy to the pharmaceutical community come largely from the ease of use, minimal sample handling and strong differences in relative scattering strengths of packaging materials, tablet excipients and the active agents. These strengths combined with the use of microscopes and fibre optics have seen a large growth of use in the pharmaceutical industry. An early worker with FT Raman quickly recognized the advantages and opportunities in the pharmaceutical industry [121]. A review by Cutmore and Skett [122] is still very valid. Although the fluorescence issue is still a problem with dispersive instruments, applications such as drug screening and polymorphism have been studied by both FT and dispersive techniques. In the area of fibre-optic coupling, microprobes and imaging dispersive technology is very much at the forefront. As with other application areas in this chapter, there is not room for a comprehensive review but a few illustrative examples are given.

##### □ NON-CONTACT *IN SITU* MEASUREMENT

For quality control of manufacturing and formulation the ability to check directly inside a polymer package produces tremendous time and cost savings. Imaging of tablets can be carried out to check the distribution and relative amounts of active agent, additives and binders present. The active drug is often an aromatic-based compound with distinctive Raman spectra whilst the other components are sugar, cellulose or inorganic-based materials. The active component itself can also have variable properties dependent on the physical form or crystallinity. These can affect dissolution rates and hence the efficacy of the drug. Drug samples, including both prescription drugs and drugs of abuse, can be measured *in situ* in clear plastic wrappings. This can be important both in the speed of analysis and in preventing sample contamination. If a microscope system is used, the laser beam can be focussed onto the surface of the tablet through the plastic packing material. The high-power-density area created provides most of the Raman scattering and therefore discriminates in favour of the tablet or powder. In addition, the scattering from the drug is usually relatively intense compared to that from the plastic material. In Figure 6.19, an example of this type of experiment is shown.



**Figure 6.19.** Raman spectra of aspirin, commercial sample of aspirin, and aspirin inside plastic wrapper.

A commercial aspirin tablet, an identical tablet wrapped in plastic and laboratory-synthesized aspirin powder all give almost identical spectra with the same accumulation times. As can be seen, the spectra of the aspirin can clearly be identified in each case. There are relative band strength differences. In the spectra the aspirin gives strong bands, the binder gives weak bands and none are present from the wrapping material. This demonstrates significant selectivity in Raman scattering experiments. This simple experiment was carried out using 30-s accumulations in a standard Raman spectrometer. It indicates the simplicity with which a compound can be identified *in situ* and provides significant information which helps both to identify a specific compound and to indicate impurities. For example, the inorganic filler in the tablet gives rise to a band at about  $1100\text{ cm}^{-1}$  which is not present in the laboratory aspirin sample and the additional band at about  $1370\text{ cm}^{-1}$  shows that the laboratory aspirin sample was not pure.

#### □ MOLECULAR SPECIFICITY

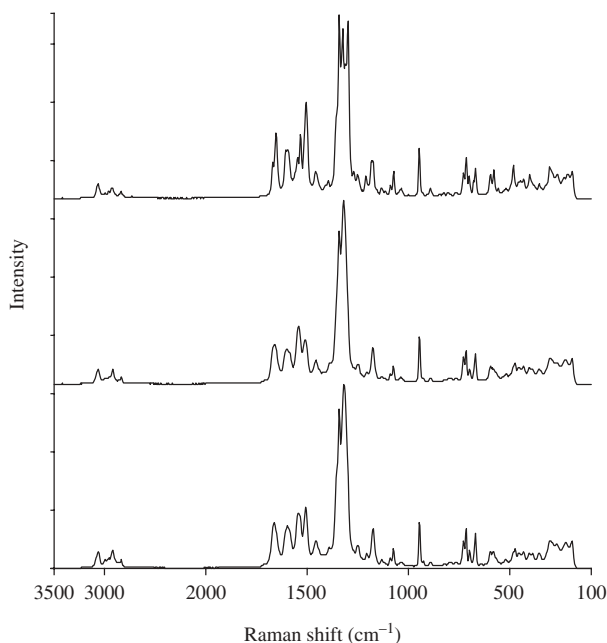
Raman scattering can be obtained from a set of drugs of abuse. Each spectrum is molecularly specific. Initial identification of a sample without the matrix is very simple by Raman scattering. However in real world samples the drugs are often in a matrix of several compounds. This matrix can cause fluorescence which swamps the image; in the case of inorganics, Raman spectroscopy can be used to identify the impurity.

#### □ POLYMORPHISM

One property which can greatly affect the efficacy of a drug is polymorphism. The term can be used in the biological and pharmaceutical worlds with totally different meanings. In most of the chemistry applications and here in pharmaceutical

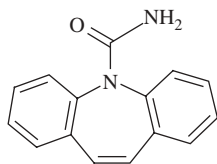
applications, McCrone's definition [123] is used to mean differing physical forms of the same molecule. Raman spectroscopy is ideally suited to studying polymorphism as the lack of sample handling minimizes the risk of converting the form during measurement as can occur with other techniques. Surprisingly, an extensive review by Threlfall [124] of analytical techniques employed to study polymorphism did not have a very large section on Raman spectroscopy. Much of what was reported was with FT Raman. Even so the technique has shown differences with polymorphs of several compounds [125–128] including the B and C forms of naphthazarin [129] and the morphological composition of cimetidine [130]. In addition to that of the active agent, the differing crystallinity of excipients such as glucose have also been recorded [131]. The strict confidentiality surrounding pharmaceutical drug structures are the composition of tablets and this means that much of this work has not been reported in the open literature. For example, a recent application note [132] on polymorphism by dispersive Raman refers only to forms A and B without identifying the drug. A review by Frank [133] contains many examples of the use of Raman spectroscopy in the study of pharmaceuticals.

Yet another example of an unnamed pharmaceutical intermediate is shown in Figure 6.20 recorded by the authors. The FT Raman spectra were recorded



**Figure 6.20.** Crystallinity in pharmaceutical intermediate: crystalline form (top); amorphous (middle); mixture of crystalline and amorphous forms (bottom).

of pure crystalline and amorphous forms of the intermediate. A suspect batch of the amorphous form was examined without opening the sampling vial. The spectrum shows evidence of crystallinity at  $\sim 1500\text{ cm}^{-1}$ . However some examples of the use of Raman spectroscopy with pharmaceuticals for which the structure is known have been published. For example, the use of Raman scattering for high throughput screening of carbamazepine (**8**) has been reported by the Novartis company [134].



(8)

Carbamazepine

## 6.8 FORENSIC APPLICATIONS

Modern developments in equipment for the detection of Raman scattering make the method very useful in the area of forensic science [135]. The main advantages of Raman scattering in forensic science are the non-invasive, non-contact nature of the method, the ready coupling of the instrumentation to microscopes so that detection of very small amounts is achieved easily, and the molecularly specific nature of Raman scattering. Both visible and NIR FT systems are applicable. In forensic science, it is usual that these are coupled either to a microscope or to a fibre-optic head so that sampling of small areas of material can be performed. In current applications, the microscope is more widely used, but the requirement to use the instrument in the field may, in certain circumstances, dictate the use of a simple, small fibre-optic-coupled head. The main advantage of using the NIR system in forensic science is reduced fluorescence, which can be a major problem with a sample in the matrix but the simpler, more flexible optics of the visible system can make this the system of choice in many applications. To this extent the advantages are very similar to those described in Section 6.3. Indeed it can be argued that forensic science is already applying those concepts described in previous sections on the micro-scale. Specific examples already quoted in this chapter are drugs, fibres and colour probes in several situations. Indeed it can be argued that the advancement of Raman technology has been a contributing factor in enabling analytical scientists to take a forensic approach to problem solving. Besides fibre identification and biological effects, where SER(R)S can be advantageous, one of the areas of significant interest to forensic science is the

identification of explosives. Nitro-group containing RDX and PETN are components of plastic explosives that have very low vapour pressure. These can be identified readily from one small particle by Raman scattering. It is possible to examine a surface such as that from a fingerprint to obtain either an image of the surface under the microscope or to map a larger area. Mapping enables the analysis of larger areas. Images of a fingerprint showing the presence of a particle of RDX have been recorded [136].

## 6.9 PLANT CONTROL AND REACTION FOLLOWING

### 6.9.1 Introduction

Whilst many applications mentioned in this chapter so far have used static, or *in situ* measurements, a growing area of interest for Raman spectroscopy is reaction following. In principle the technique is ideal, being non-invasive, able to detect from within glass vessels and aqueous media, and able to carry out monitoring at long distances. Published reports of industrial applications have until recently been relatively sparse. Many have covered laboratory trials or proof of principle. This has been due to several reasons. Fluorescence makes the technique very application-specific. If an instrument is developed to monitor a specific reaction, it does not follow that it can be easily transferred to other applications. The instrumentation was until recently very large, expensive, required specific environmental conditions, i.e. dark rooms, laser interlocked doors. With the introduction of modern variable filter instruments and FT spectrometers, the instrumentation has become much more user friendly and adaptable. Flexibility of application has increased with lasers sources at 785 and 1064 nm and in the UV, thus reducing fluorescence for reaction following. The portability and increased simplicity of the instruments has also opened up the possibility of on-plant monitoring. The latter is somewhat under-reported. This tends to be due to companies wishing to maintain the commercial edge gained from greater efficiencies achieved by tighter plant control. The number of reported examples of reaction following and plant monitoring is increasing. Two excellent reviews have been published [137, 138] on the parameters to be aware of and potential pitfalls in introducing Raman spectroscopy in an industrial plant. A few typical applications are given.

### 6.9.2 Electronics and Semiconductors

Probably one of the biggest quality control (QC) applications [139, 140] for Raman spectroscopy is monitoring of the protective diamond-like films (DLF) for computer hard disks. Information on hydrogen content,  $sp^2/sp^3$  ratios and

long-range ordering is available from the Raman spectra. Instruments solely dedicated to these measurements can automatically predict the tribological qualities of the films [138, 141]. QC techniques have been established for the physical and chemical characterization of semiconductors, which can include crystal size and form, dopant levels, stress and strain. This is a major topic in itself for which there are several reviews [142–144] and which is also discussed in Section 6.6. Another feature of process monitoring in this industry is in the deposition and/or growth of thin films. Raman spectroscopy is particularly applicable when the process occurs under vacuum or at elevated temperatures. This could be potentially important for monitoring novel heterostructures [145]. The growth of InSb on Sb(1 1 1) has been studied [146] with thicknesses of 0–40 nm. The growth of ZnSe on GaAs at 300 °C followed by capping with Se has been reported [147]. This was followed by crystallization studies of the Se layer. Other studies [148] have included the nitridation of ZnSe on the GaAs and the growth of CdS on InP(1 0 0). This industry probably makes the largest use of process and QC applications of Raman spectroscopy. It is an application which is extremely important to modern life and technology and yet does not greatly feature in conventional literature on analytical chemistry.

### 6.9.3 $\text{PCl}_3$ Production Monitoring

If a plant analyst was asked which reactions would cause the largest problems in monitoring, then elemental phosphorous combined with chlorine in a boiling liquid would feature high on the list. Yet this, the production of  $\text{PCl}_3$ , is one of the best known examples of Raman on-line monitoring [149] developed by Freeman *et al.* The levels of chlorine have to be maintained to prevent the production of  $\text{PCl}_5$ . Using a sampling loop, an FT Raman spectrometer and fibre bundles with laser powers of 2 W, and with 140 scans and  $16\text{ cm}^{-1}$  resolution detection levels of <1% for  $\text{P}_4$  and  $\text{Cl}_2$  were attained. Side products of  $\text{POCl}_3$  and  $\text{SbCl}_3$  were also monitored but these degraded under the high laser power. Gervasio and Pelletier [150] refined the measurement with a CCD-dispersive system, a 785 nm laser and a direct insertion probe.

### 6.9.4 Anatase and Rutile Forms of Titanium Dioxide

One of the earliest publications on plant control is the monitoring of the physical form of titanium dioxide, a very bright and white commonly used pigment. However the pigment exists in different physical forms. The major ones being anatase and rutile. The rutile form, having a higher opacity, is more commonly used. Both forms have very distinctive bands in the Raman spectrum (see Figure 6.3). The anatase form has bands at 640, 515, 395 and  $145\text{ cm}^{-1}$  whilst the rutile bands appear at 610 and  $450\text{ cm}^{-1}$ . These bands have been used to quantitatively measure 1% of anatase in rutile with enough

accuracy for semi-automated plant control [151]. The greatest difficulty with this measurement was the dusty environment inside the production plant which resulted in major engineering problems. These problems and their solution have been colourfully described at length by Everall *et al.* [137].

### 6.9.5 Polymers and Emulsions

As described in Section 6.4, one of the simplest reactions to follow by Raman spectroscopy is the loss of the  $>C=C<$  bond. This gives very clear and strong bands in simple monomers such as acrylates, vinyl acetates and styrene. There are numerous literature references covering a range of applications from the simple to the complex. Styrene (S) and methylmethacrylate (MMA) have been studied in a reaction cell [152], homopolymerizations of MMA and butyl acrylate (BuA) have been monitored by FT Raman in laboratory reactors [153] and an analysis of a complex quaternary polymer (S/BuA/MMA/cross-linker) has been carried out [154] to show the consumption of monomers followed by the composition of the resultant copolymer. It would be easy to think that the  $>C=C<$  bond band could be monitored quantitatively directly and this can indeed be the case [152, 153]. However, changes in laser intensity, spectrometer response and inhomogeneity can lead to the band having to be normalized. This is usually carried out by choosing a band not affected by the reaction being followed. Unfortunately this simplistic approach cannot be used.

Several workers [152, 155] have reported intensity changes in bands, used for reference purposes, between the monomer and polymer states. This has been discussed in depth by Everall [156]. Whilst these systems can be monitored quantitatively, similar reactions taking place in emulsions require even greater care. The monomer can exist as droplets, dissolved in water, as micelles or in the polymer phase. The band intensity and wavenumber position can be affected by which phase the monomer is in. Temperature and pressure changes can affect both the spectrum and the phase in which the monomer resides. Equally importantly, the detection of the drops can be affected by the size relative to the wavelength of the laser exciting line (see particle size effects, Chapter 2). These factors need to be taken into consideration but should not prevent analysis taking place, as a published application [157] monitoring latex emulsion polymerization has shown. Vinyl and acrylate monomers have been largely described here but other systems have also been reported such as cyanate esters [158], epoxies [159], melamine-formaldehydes [160], polyimides [161] and polyurethanes [162]. All the applications described so far have taken place largely in bulk in reaction vessels. Raman spectroscopy has developed in these applications through the use of direct probes and/or coupling with fibre optics which in the case of visible laser sources can be monitored at distances of up to several metres. Another area of application employing *in situ* analysis by Raman spectroscopy is in extruders, fibres and films. In these cases the physical



properties of the polymer can be studied as well as the chemical composition. Early work by Hendra [163], taking advantage of polarized Raman spectroscopy, analysed polymers in a lab-scale extruder for information on crystallinity, chain conformation and orientation. Modern instrumentation and fibre optics developments have enabled similar measurements to be carried out *in situ* on pilot plant and full scale production facilities. Recently Chase has also taken advantage of polarized Raman spectroscopy to study fibres at varying points of the drawing process and has carried out extensive studies of fibres on spinning rigs [164, 165].

Similar measurements would appear to be applicable to polymer film production. The measurements are quite complex as the morphological properties can develop in three dimensions. Farquharson and Simpson [166] demonstrated the feasibility with a dispersive spectrometer and a 5 m fibre bundle in a first-reported Raman on-line analysis of polymer film production. Since then Everall has carried out extensive work on the composition of polyester film on a moving production line using imaging fibre probes coupled though 100 m of fibre [167, 168]. One of the features discovered in this work was the difficulty in handling fluorescence in a moving film compared to static measurements. When a polymer film is static in the beam, low levels of fluorescence can be burnt out (photobleached). With a moving film the sample is rapidly refreshed maintaining the level of fluorescence. Moving from visible excitation towards 785 nm can reduce these effects but Everall found that addition of reclaimed polymer to the stream was a cause of fluorescence [156]. Monitoring polymer film of various types is an application of plant control where Raman spectroscopy would have been expected to have wide use. The lack of literature could be due to commercial sensitivity.

### 6.9.6 Pharmaceutical Industry

The pharmaceutical industry has many potential applications as described in Section 6.7. The minimal sample handling and the ability to 'see' into polymer containers would be expected to lead to numerous QC applications. Instrument manufacturers claimed expanding sales due to interest in polymorphism alone. Yet little literature, apart from manufacturers' application notes, is available for on-plant applications. Again it is probably commercial sensitivity which is the cause. Interested readers should consult the later references in Section 6.7.

### 6.9.7 Fermentations

Biotechnology and bioreactors are a fast growing area of technology. The potential advantage of Raman spectroscopy is the ability to study aqueous systems, though fluorescence and particulates are still potential problems. Little was reported prior to the introduction of lasers in the red end of the spectrum. Shaw *et al.* [169] have analysed glucose fermentation with a fibre optic coupled 785 nm laser. They extracted and filtered the liquid to remove yeast cells, which, though not a direct measurement, demonstrated the potential of the technique.

By employing PLS techniques and other modelling techniques, including neural networks, glucose and ethanol contents were predicted with errors of  $\sim 4\%$ .

### 6.9.8 Gases

Raman spectroscopy of gases is not an industrial application which readily springs to mind yet, as stated in Chapter 2, some of the earliest Raman spectroscopy was carried out on gases and vapours in inclusions in minerals and rock. The low sensitivity of Raman spectroscopy to gases, due to the low scattering cross-section and few molecules in a given volume, would appear to reduce the applicability. However these drawbacks have been overcome by using special cells, instruments or remote sensing techniques such as light source techniques similar to radar known as Raman LIDAR [170]. A simple case which demonstrates the sensitivity of Raman spectroscopy to simple molecules is the interference that can occur in weak Raman spectra from fluorescent room lights. Here, sharp emission bands are recorded which can be mistaken for the sample and would certainly cause problems with multivariate analysis routines. The pattern varies with the laser exciting line used. The relatively weak spectra were enhanced by using multipass cells [141] and placing these inside the laser cavity. Quantitative measurements have been made of CO, CO<sub>2</sub>, H<sub>2</sub>, H<sub>2</sub>O, N<sub>2</sub>, N<sub>2</sub>O, NH<sub>3</sub> and hydrocarbons using a simple spectrometer constructed from simple components and an intracavity gas cell. The Raman analyser, known as a 'Regap' analyser, has been described by de Groot and Rich [171] for measuring and controlling atmospheres in a steel treatment furnace. Large scale QC methods have been devised [172], but methods using Raman microscopes are also used. The applications include accelerator devices for vehicle air bags and degradation of pharmaceuticals inside package products [173]. In each of these applications it is the *in situ* aspects of Raman spectroscopy which overcome the other apparent limitations.

### 6.9.9 Catalysts

The study of surfaces under an aqueous phase in a glass container may be a nightmare for an infrared spectroscopist but will cause little difficulty for a Raman spectroscopist. At an American Chemical Society (ACS) Conference in 2000, statistics were produced which showed that Raman-based catalysts studies were being published at a rate in excess of 300 a year. Clearly we cannot cover a field of that size adequately in this book but it is well covered in other publications [174]. We will highlight the applicability of Raman spectroscopy in this field and point the interested reader to further material. The simplest advantages have already been stated. Raman spectroscopy can study systems inside vessels over a range of temperatures and pressures. As many catalyst studies are carried out at several hundred degrees centigrade, this is a major

factor. Typical studies are in the automotive industry where catalytic converters for vehicle exhausts operate most efficiently at higher temperatures [175]. The crystal structure of metal oxides and metal co-ordination chemistry is a wide field of study. Metals commonly encountered are platinum, palladium, ruthenium, titanium, uranium, vanadium and zirconium. Alumina- and silica-based catalysts are of continuing wide interest. Many of these materials contain a chromophore which opens up the field to resonance Raman studies. This then has the added advantage of increased selective sensitivity. One of the problems regularly encountered in Raman spectroscopy is fluorescence. There has been an increase in the use of UV laser sources for Raman spectroscopy in this area to overcome fluorescence and also to increase sensitivity [176]. Besides complete reaction following, catalytic partial oxidation is important in industry for production of materials such as alcohols. A typical case is the production of methanol from methane [177].

One of the largest areas of study, of course, is in electrochemical reactions, particularly studies on electrode surfaces. In addition to the normal Raman and resonance Raman advantages in this area, the surface enhance effect (SERS) is of great importance. Indeed as previously shown, the SERS effect was first observed on an electrode surface. This coupled to resonance to create the SERRS effect makes Raman a very powerful tool in this area. Very brief references have been made to an ocean of work. The bibliography will point the reader to much more detailed work.

## 6.10 SUMMARY

This chapter whilst giving only a flavour of the vast range of applications in which Raman spectroscopy has been utilized should lead the reader to realize the specific niche which the technique still occupies. This chapter, together with the previous chapters, shows that, although Raman instruments are not as generic as for some techniques, care in matching the instrument and accessories to a specific application can create a very powerful specific tool which can be of use to both the expert spectroscopist and the general analyst. The next chapter leads into where the technique can yield even more information, albeit requiring, in some cases but not all, expensive, specialist equipment.

## REFERENCES

### Inorganics and Minerals

1. M. Yoshikawa and N. Nagai, in: *Handbook of Vibrational Spectroscopy*, J. Chalmers and P. Griffiths (eds), vol. 4, John Wiley & Sons, Inc., New York, 2001, pp. 2593–2600.
2. M.S. Dresselhaus, G. Dresselhaus, M.A. Pimenta and P.C. Eklund, in: *Analytical Applications of Raman Spectroscopy*, M.J. Pelletier (ed.), Blackwell Science, Oxford, 1999, pp. 367–434.

3. P.J. Hendra, in: *Modern Techniques in Raman Spectroscopy*, J.J. Laserna (ed.), John Wiley & Sons, Inc., New York, 1996, p. 94.
4. P. Dhamelincourt, F. Wallart, M. LeClerq, A.T. N'Guyon and D.O. Landon, *Anal. Chem.*, **51**, 414A (1979).
5. E.S. Etz, G.J. Rosasco and W.C. Cunningham, in: *Environmental Analysis*, G.W. Ewing (ed.), Academic Press, New York, 1977, p. 295.
6. C. Beny, J.M. Prevosteau and M. Delhaye, *L'actualité chimique*, **April** 49 (1980).
7. C.J. Rosasco, *Proceedings of the 6th International Conference on Raman Spectroscopy*, Heyden, London, 1978.
8. M. Martoja, V.T. Tue and B. Elkaim, *J. Exp. Mar. Bio. Ecol.*, **43**, 251 (1980).
9. *Internet J. Vib. Spectrosc.* [www.ijvs.com].
10. A. Wang, J. Han and L. Guo, *Appl. Spectrosc.*, **48**, 8 (1994).
11. R.A. Nyquist, C.L. Putzig and M.A. Leugers, *IR and Raman Spectral Atlas of Inorganic Compounds and Organic Salts*, Academic Press, 1997.
12. E.L. Varetto and E.J. Baran, *Appl. Spectrosc.*, **48**, 1028 (1994).
13. D.H.M. Edwards and H.J. Schnubel, *Rev. Gemmol.*, **52**, 11 (1977).
14. Y. Kawakami, J. Yamamoto and H. Kagi, *Appl. Spectrosc.*, **57**, 1333–1339 (2003).
15. J. Popp, N. Tarcea, W. Kiefer, M. Hilchenbach, N. Thomas, S. Hofer and T. Stuffer, *Proceedings of the First European Workshop on Exo-/Astr-Biology ESA SP-496*, 2001.
16. R. Frost, T. Klopprogge and J. Schmidt, *Internet J. Vib. Spectrosc.* [www.ijvs.com], **3**, 4, 1.
17. D.R. Lombardi, C. Wang, B. Sun, A.W. Fountain III, T.J. Vickers, C.K. Mann, F.R. Reich, J.G. Douglas, B.A. Crawford and F.L. Kohlasch, *Appl. Spectrosc.*, **48**, 875–883 (1994).
18. K. Williams, *Spectroscopy Innovations*, vol. 6, Renishaw Ltd, 2000.
19. D. Fisher and R.A. Spits, *Gems and Gemology*, **Spring** 42 (2000).
20. H.F. Shurvell, L. Rintoul and P.M. Fredericks, *Internet J. Vib. Spectrosc.* [www.ijvs.com], **5**, 5, 2.
21. A. Peipetis, C. Vlattas and C. Galiotis, *J. Raman Spectrosc.*, **27**, 519 (1996).
22. H.G.M. Edwards, M.J. Falk, M.G. Sibley, J. Alvarez-Benedi and F. Rull, *Spectrochim. Acta A*, **54**, 903 (1998).
23. R.J.H. Clark, in: *Handbook of Vibrational Spectroscopy*, J. Chalmers and P. Griffiths (eds), vol. 4, John Wiley & Sons, Inc., New York, 2001, p. 2977.
24. F.R. Perez, H.G.M. Edwards, A. Rivas and L. Drummond, *J. Raman Spectrosc.*, **30**, 301 (1999).
25. J. Zuo, C. Xu, C. Wang and Z. Yushi, *J. Raman Spectrosc.*, **30**, 1053 (1999).
26. M.L. Dele, P. Dhamelincourt, J.P. Poroit and H.J. Schnubel, *J. Mol. Struct.*, **143**, 135 (1986).
27. R.J.H. Clark, M.L. Curri and C. Largana, *Spectrochim. Acta*, **53A**, 597 (1997).
28. L.I. McCann, K. Trentleman, T. Possley and B. Golding, *J. Raman Spectrosc.*, **30**, 121 (1999).
29. H.G.M. Edwards, D.W. Farewell and A. Quye, *J. Raman Spectrosc.*, **28**, 243 (1997).
30. H.G.M. Edwards, D.E. Hunt and M.G. Sibley, *Spectrochim. Acta*, **54**, 745 (1998).
31. E.A. Carter and H.G.M. Edwards, in: *Infrared and Raman Spectroscopy of Biological Materials*, H.-U. Gramlich and B. Yan (eds), Marcel Dekker, New York, 2001.

32. J. Chalmers and P. Griffiths (eds), *Handbook of Vibrational Spectroscopy*, vol. 4, John Wiley & Sons, Inc., New York, 2001.
33. P.J. Hendra and J.K. Agbenyega (eds), *The Raman Spectra of Polymers*, Wiley, 1993.
34. B. Schrader, *Raman/Infrared Atlas of Organic Compounds*, 2nd Edition, Wiley-VCH, Weinheim, 1989.
35. A. Garton, D.N. Batchelder and C. Cheng, *Appl. Spectrosc.*, **47**(7), 922 (1993).
36. J.M. Chalmers and N.J. Everall, in: *Polymer Characterisation*, B.J. Hunt and M.I. James (eds), Blackie Academic, Glasgow, 1993.
37. S.W. Cornell and J.L. Koenig, *Macromolecules*, **2**, 540 (1969).
38. J.A. Frankland, H.G.M. Edwards, A.F. Johnson, I.R. Lewis and S. Poshachinda, *Spectrochim. Acta*, **47A**, 1511 (1991).
39. K.D.O. Jackson, M.J.R. Loadman, C.H. Jones and G. Ellis, *Spectrochim. Acta*, **46A**, 217 (1990).
40. K. Tashiro, Y. Ueno, A. Yoshioka, F. Kaneko and M. Kobayashi, *Macromol. Symp.*, **114**, 33 (1999).
41. K. Tashiro, S. Sasaki, Y. Ueno, A. Yoshioka and M. Kobayashi, *Korea Polym. J.*, **8**, 103 (2000).
42. N.J. Everall, J.M. Chalmers, L.H. Kidder, E.N. Lewis, M. Schaeberle and I. Levin, *Polym. Mater. Sci. Eng.*, **82**, 398–399 (2000).
43. H.-J. Sue, J.D. Earls, R.E. Hefner Jr., M.I. Villarreal, E.I. Garcia-Meitin, P.C. Yang, C.M. Cheetham and C.J. Plummer, *Polymer*, **39**, 4707 (1998).
44. J.R. Walton and K.P.J. Williams, *Vib. Spectrosc.*, **1**, 239 (1991).
45. K.E. Chike, M.L. Myrick, R.E. Lyon and S.M. Angel, *Appl. Spectrosc.*, **47**, 1631 (1993).
46. M. Kawagoe, M. Takeshima, M. Nomiya, J. Qiu, M. Morita, W. Mizuno and H. Kitano, *Polymer*, **40**, 1373 (1999).
47. M. Kawagoe, S. Hashimoto, M. Nomiya, J. Qiu, M. Morita, W. Mizuno and H. Kitano, *J. Raman Spectrosc.*, **30**, 913 (1999).
48. D.L. Gerrard and W.F. Maddams, *Macromolecules* **8**, 55 (1975).
49. A. Baruya, D.L. Gerrard and W.F. Maddams, *Macromolecules*, **16**, 578 (1983).
50. E.D. Owen, M. Shah, N.J. Everall and M.V. Twigg, *Macromolecules*, **27**, 3436 (1994).
51. H.E. Schaffer, R.R. Chance, R.J. Sibley, K. Knoll and R.R. Schrock, *J. Phys. Chem.*, **94**, 4161 (1991).
52. J.M. Chalmers and G. Dent, in: *Industrial Analysis with Vibrational Spectroscopy*, Royal Society of Chemistry, London, 1997.
53. I. Persaund and W.E.L. Grossman, *J. Raman Spectrosc.*, **24**, 107 (1993).
54. M. Majoube and M. Henry, *Spectrochim. Acta A*, **47**, 1459 (1991).
55. K. Neipp, Y. Wang, R.R. Desari and M.S. Field, *Appl. Spectrosc.*, **49**, 780 (1995).
56. C. Rodger, W.E. Smith, G. Dent, M. Edmondson, *J. Chem. Soc. Dalton Trans.*, **5**, 791–799 (1996).
57. D. Graham, W.E. Smith, A.M.T. Lineacre, C.H. Munro, N.D. Watson and P.C. White, *Anal. Chem.*, **69**, 4703–4707 (1997).
58. D. Graham, B.J. Mallinder and W.E. Smith, *Angewandte Chemie Int. Ed. Engl.*, **6**, 1061–1063 (2000).

59. D. Graham, B.J. Mallinder and W.E. Smith, *Biopolymers(Biospectroscopy)*, **112**, 1103–1105 (2000).
60. D. Bourgeois and S.P. Church, *Spectrochim. Acta A*, **46**, 295 (1990).
61. N. Everall, *Spectrochim. Acta A*, **49**, 727–730 (1993).
62. G. McGeorge, R.K. Harris, A.M. Chippendale and J.F. Bullock, *J. Chem. Soc. Perkin Trans.*, **2**, 1733 (1996).
63. G. McGeorge, R.K. Harris, A.S. Bastanov, A.V. Churakov, A.M. Chippendale, J.F. Bullock and Z. Gan, *J. Chem. Soc. Perkin Trans.*, **102**, 3505–3513 (1998).
64. P.C. White, C. Rodger, V. Rutherford, W.E. Smith and M. Fitzgerald, *SPIE*, **3578**, 77 (1998).
65. P.C. White, C.H. Munro and W.E. Smith, *Analyst*, **121**, 835 (1996).
66. P.C. White, C. Rodger, V. Rutherford, D. Broughton and W.E. Smith, *Analyst*, **123**, 1823 (1998).
67. J.A.G. Drake (ed.), *Chemical Technology in Printing Systems*, Royal Society of Chemistry, London, 1993.
68. C. Rodger, *The Development of SERRS as a Quantitative and Qualitative Analytical Technique*, Ph.D. Dissertation, University of Strathclyde, Glasgow, 1997.
69. C. Rodger, G. Dent, J. Watkinson and W.E. Smith, *Appl. Spectrosc.*, **54** (2000).
70. D.R. Armstrong, J. Clarkson and W.E. Smith, *J. Phys. Chem.*, **99**, 17825 (1995).
71. K.I. Mullen, D.X. Wang, L.G. Crane and K.T. Carron, *Anal. Chem.*, **64**, 930–936 (1992).
72. H. Zollinger, *Colour Chemistry*, VCH, Weinheim, 1991.
73. K. Venkataraman, *The Analytical Chemistry of Synthetic Dyes*, John Wiley & Sons, New York, 1977.
74. A. Tsumura, H. Koezuka and T. Ando, *Appl. Phys. Lett.*, **49**, 1210 (1986).
75. J.H. Burroughs, C.A. Jones and R.H. Friend, *Nature*, **335**, 137 (1988).
76. Z. Bao, J.A. Rodgers and H.E. Katz, *J. Mater. Chem.*, **9**, 1895 (1999).
77. G. Yu, J. Gao, J.C. Hummelen, F. Wudl and A.J. Heeger, *Science*, **270**, 1789 (1995).
78. J.H. Burroughs, D.D.C. Bradley, A.R. Brown, R.N. Marks, K. Mackay, R.H. Friend, P.L. Burns and A.B. Holmes, *Nature*, **347**, 539 (1990).
79. R.H. Friend, R.W. Gymer, A.B. Holmes, J.H. Burroughs, R.N. Marks, C. Taliani, D.D.C. Bradley, D.A. Dos Santos, J.L. Brédas, M. Lögdlund and W.R. Salaneck, *Nature*, **397**, 121 (1999).
80. T.A. Skotheim, R.L. Elsenbaummer and J.R. Reynolds (eds), *Handbook of Conducting Polymers*, Marcel Dekker, New York, 1997.
81. N.S. Sariciftci (eds), *Primary Photoexcitations in Conjugated Polymers: Molecular Exciton versus Semiconductor Band Model*, World Scientific, Singapore, 1997.
82. H. Keiss (ed.), *Conjugated Conducting Polymers*, Springer-Verlag, Berlin, 1992.
83. Y. Shirota, *J. Mater. Chem.*, **10**, 1 (2000).
84. Aldrich Online Chemical Catalogue, [www.sigmaaldrich.com/Brands/Aldrich/Polymer\\_Products/Specialty\\_Areas.html](http://www.sigmaaldrich.com/Brands/Aldrich/Polymer_Products/Specialty_Areas.html).
85. H. Becker, H. Spreitzer, W. Kreuder, E. Kluge, H. Schenk, I. Parker and Y. Cao, *Adv. Mater.*, **12**, 42 (2000).
86. S. Bernard and P. Yu, *Adv. Mater.*, **12**, 48 (2000).
87. W.P. Su, J.R. Schrieffer and H.J. Heeger, *Phys. Rev. B*, **22**, 2099 (1980).
88. W.P. Su and J.R. Schrieffer, *Proc. Natl. Acad. Sci. USA*, **77**, 5626 (1980).
89. J.L. Brédas, R.R. Chance and R. Sibley, *Mol. Cryst. Liq. Cryst.*, **77**, 253 (1981).

90. M. Fleischmann, P.J. Hendra and A.J. McQuillan, *Chem. Phys. Lett.*, **26**, 163 (1974).
91. M. Yoshikawa and N. Ngai, in: *Handbook of Vibrational Spectroscopy*, J. Chalmers and P. Griffiths (eds), vol. 4, John Wiley & Sons, New York, 2001, p. 2604.
92. M.D. Schaeberle, D.D. Tuschel and P.J. Treado, *Appl. Spectrosc.*, **55**, 257–266 (2001).
93. F. Cerdeira, T.A. Fjeldly and M. Cardona, *Phys. Rev. B*, **8**, 4734 (1973).
94. M. Yoshikawa, K. Agawam, N. Morita, T. Matsunobe and H. Ishida, *Thin Solid Films*, **310**, 167 (1997).
95. J.-H. Kim, S.-H. Seo, S.-M. Yun, H.-Y. Chang, K.-M. Lee and C.-K. Choi, *Appl. Phys. Lett.*, **68**, 1507 (1996).
96. S. Nakashima and H. Harima, in: *Handbook of Vibrational Spectroscopy*, J. Chalmers and P. Griffiths (eds), vol. 4, John Wiley & Sons, Inc., New York, 2001, pp. 2637–2650.
97. F.H. Pollak and R. Tsu, *Proc. SPIE*, **452**, 26 (1984).
98. S. Nakshima and M. Hangyo, *Trans. IEEE*, **QE-25**, 965 (1989).
99. P. Dhamelinourt and S. Nakshima, in: *Raman Microscopy*, G. Turrel and J. Corset (eds), Academic Press, London, 1996.
100. H.-U. Gramlich and B. Yan (eds), *Infrared and Raman Spectroscopy of Biological Materials*, Marcel Dekker, 2001.
101. P.T.C. Freire, in: *Proceedings of the International Conference on Raman Spectroscopy*, S.L. Zhang and B.F. Zhu (eds), John Wiley & Sons, 2000, p. 440.
102. K.C. Schuster, I. Reese, E. Urlab, J.R. Gapes and B. Lendl, *Anal. Chem.*, **72**, 5529 (2000).
103. T.A. Alexander, P.M. Pelligrino and J.B. Gillespie, *Appl. Spectrosc.*, **57**, 1340–1345 (2003).
104. J.P. Wold, B.J. Marquardt, B.K. Dable, D. Robb and B. Hatlen, *Appl. Spectrosc.*, **58**, 395–403 (2004).
105. G.D. Sockalingum, H. Lamfarraj, A. Beljebbar, P. Pina, M. Delavenne, F. Witthuhn, P. Allouch and M. Manfait, *SPIE*, **3608**, 185 (1999).
106. C. Arcangeli and S. Cannistraro, *Biopolymers*, **57**, 179–186 (2000).
107. O. Piot, J.C. Autran and M. Manfait, *J. Cereal Sci.*, **34**, 191–205 (2001).
108. H. Matsi and S. Pan, *J. Phys. Chem. B*, **104**, 8871 (2000).
109. J. Zheng, Q. Zhou, Y. Zhou, T. Lou, T.M. Cotton and G. Chumanov, *J. Electroanal. Chem.*, **530**, 75–81 (2002).
110. M. Manfait, P. Lamaze, H. Lamfarraj, M. Pluot and G.D. Sockalingum, *Biomed. Spec.*, *SPIE*, **3918**, 153 (2000).
111. C.J. Frank, R.L. McCreery and D.C. Redd, *Anal. Chem.*, **67**, 777–783 (1995).
112. E. Atherton, D.L. Clive and R.C. Sheppard, *J. Am. Chem. Soc.*, **97**, 6584 (1975).
113. B. Yan, H.-U. Gremlich, S. Moss, G.M. Coppola, Q. Sun and L. Liu, *J. Comb. Chem.*, **1**, 46–54 (1999).
114. C.-D. Chang and J. Meisenhofer, *Int. J. Protein Res.*, **11**, 246 (1978).
115. E. Atherton, H. Fox, D. Harkiss, J.C. Logan, R.C. Sheppard and B.J. Williams, *J. Chem. Soc. Chem. Commun.*, **537** (1978).
116. J. Ryttersgaard, B. Due Larsen, A. Holm, D.H. Christensen and O. Faurskov Nielsen, *Spectrochim. Acta A*, **53**, 91–98 (1997).

117. D.E. Pivonka, K. Russell and T.W. Gero, *Appl. Spectrosc.*, **50**, 1471 (1996).
118. D.E. Pivonka, D.L. Palmer and T.W. Gero, *Appl. Spectrosc.*, **53**, 1027 (1999).
119. D.E. Pivonka, *J. Comb. Chem.*, **2**, 33–38 (2000).
120. Application Note, In-situ Analysis of Combinatorial Beads by Dispersive Raman Spectroscopy, *Nicolet*, **AN-00121** (2001).
121. G. Ellis, P.J. Hendra, C.M. Hodges, T. Jawhari, C.H. Jones, P. LeBarazer, C. Passingham, I.A.M. Royaud, A. Sanchez-Blazquez and G.M. Warnes, *Analyst*, **114**, 1061–1066 (1989).
122. E.A. Cutmore and P.W. Skett, *Spectrochim. Acta*, **49**, 809–818 (1993).
123. W.C. McCrone, in: *Physics and Chemistry of the Organic Solid State*, D. Fox, M.M. Labes and A. Weissberger (eds), vol. II, Interscience, New York, 1965, p. 275.
124. T.L. Threlfall, *Analyst*, **120**, 2435 (1995).
125. J. Anwar, S.E. Tarling and P. Barnes, *J. Pharm. Sci.*, **78**, 337 (1989).
126. G.A. Neville, H.D. Beckstead and H.F. Shurvell, *J. Pharm. Sci.*, **81**, 1141 (1992).
127. C.M. Deeley, R.A. Spragg and T.L. Threlfall, *Spectrochim. Acta*, **47**, 1217 (1991).
128. A.H. Tudor, M.C. Davies, C.D. Melia, D.G. Lee, R.C. Mitchell, P.J. Hendra and S.F. Church, *Spectrochim. Acta*, **47**, 1389 (1991).
129. S. Paul, C.H.J. Schutte and P.J. Hendra, *Spectrochim. Acta*, **46**, 323 (1990).
130. G. Jalsovszky, O. Egyed, S. Holly and B. Hegedus, *Appl. Spectrosc.*, **49**(8), 1142 (1995).
131. P.J. Hendra, in: *Modern Techniques in Raman Spectroscopy*, J.J. Laserna (ed.), Wiley, 1996, p. 89.
132. Application Note, Polymorph Analysis by Dispersive Raman Spectroscopy, *Nicolet*, **AN119** (2001).
133. C. Frank, in: *Analytical Applications of Raman Spectroscopy*, M.J. Pelletier (ed.), Blackwell Science, Oxford, 1999, pp. 224–275.
134. R. Hilfiker, J. Berghausen, C. Marcolli, M. Szelagiewicz and U. Hofmeier, *Eur. Pharm. Rev.*, **2**, 37–43 (2002).
135. C. Cheng, T.E. Kirkbride, D.N. Bachelder, R.I. Lacey and T.G. Sheldon, *J. Forensic Sci.*, **40**, 31 (1995).
136. W.E. Smith, C. Rodger, G. Dent and P.C. White, in: *Handbook of Raman Spectroscopy*, I.R. Lewis and H.G. Edwards (eds), Marcel Dekker, 2001.
137. N.J. Everall, I.M. Clegg and P.W.B. King, in: *Handbook of Vibrational Spectroscopy*, J. Chalmers and P. Griffiths (eds), vol. 4, John Wiley & Sons, 2001, pp. 2770–2801.
138. I.R. Lewis, in: *Handbook of Raman Spectroscopy*, I.R. Lewis and H.G.M. Edwards (eds), Marcel Dekker, New York, 2001, pp. 919–974.
139. L.S. Plano and F. Adar, *Proc. SPIE*, **822**, 52 (1987).
140. H.C. Tsai and D.B. Bogoy, *J. Vac. Sci. Technol. A*, **5**, 3287 (1987).
141. F. Adar, R. Geiger and J. Noonan, *Appl. Spectrosc. Rev.*, **32**, 45 (1997).
142. F.H. Pollack, in: *Analytical Raman Spectroscopy*, J.G. Grasselli and B.J. Bulkin (eds), John Wiley & Sons, New York, 1991, pp. 137–221.
143. I. de Wolf, in: *Analytical Applications of Raman Spectroscopy*, M.J. Pelletier (ed.), Blackwell Science, Oxford, 1999, pp. 435–472.
144. S. Nakashima and H. Harima, in: *Handbook of Vibrational Spectroscopy*, J. Chalmers and P. Griffiths (eds), vol. 4, John Wiley & Sons, 2001, pp. 2637–2656.



145. V. Wagner, W. Ritcher, J. Geurtus, D. Drews and D.R.T. Zahn, *J. Raman Spectrosc.*, **27**, 265 (1996).
146. V. Wagner, D. Drews, N. Esser, D.R.T. Zahn, J. Geurtus and W. Ritcher, *J. Appl. Phys.*, **75**, 7330 (1994).
147. D. Drews, A. Schneider, D.R.T. Zahn, D.A. Evans and D. Wolfframm, *Appl. Surf. Sci.*, **104/105**, 485 (1996).
148. D.R.T. Zahn, *Appl. Surf. Sci.*, **123/124**, 276 (1998).
149. J.J. Freeman, D.O. Fisher and G.J. Gervasio, *Appl. Spectrosc.*, **47**, 1115 (1993).
150. G.J. Gervasio and M.J. Pelletier, *At-Process*, **3**, 7 (1997).
151. J.P. Besson, P.W.B. King, T.A. Wilkins, M. McIvor and N. Everall, European Patent Application EP 0 767 222 A2, 'Calcination of Titanium Dioxide' (1996).
152. E. Gulari, K. McKeigue and K.Y.S. Ng, *Macromolecules*, **17**, 1822 (1984).
153. J. Clarkson, S.M. Mason and K.P.J. Williams, *Spectrochim. Acta*, **47A**, 1345 (1991).
154. N. Everall and B. King, *Macromolecules*, **141**, 103 (1999).
155. C. Wang, T.J. Vickers, J.B. Schlenoff and C.K. Mann, *Appl. Spectrosc.*, **46**, 1729 (1992).
156. N. Everall, in: *Analytical Applications of Raman Spectroscopy*, M.J. Pelletier (ed.), Blackwell Science, Oxford, 1999, pp. 127–192.
157. C. Bauer, B. Anram, M. Agnely, D. Charmot, J. Sawatzki, N. Dupy and J.-P. Huvenne, *Appl. Spectrosc.*, **54**, 528 (2000).
158. J.B. Cooper, T.M. Vess, L.A. Campbell and B.J. Jensen, *J. Appl. Polym. Sci.*, **62**, 135 (1996).
159. J.F. Aust, K.S. Booksh, C.M. Stellman, R.S. Parnas and M.L. Myrick, *Appl. Spectrosc.*, **51**, 247 (1997).
160. M.L. Scheepers, J.M. Gelan, R.A. Carleer, P.J. Adriaesens, D.J. Vanderzande, B.J. Kip and P.M. Brandts, *Vib. Spectrosc.*, **6**, 55 (1993).
161. J.B. Cooper, K.L. Wise and B.J. Jensen, *Anal. Chem.*, **69**, 1973 (1997).
162. L. Xu, C. Li and K.Y.S. Ng, *J. Phys. Chem. A*, **104**, 3952 (2000).
163. P.J. Hendra, D.B. Morris, R.D. Sang and H.A. Willis, *Polymer*, **23**, 9 (1982).
164. D.B. Chase, in: *XVth International Conference on Raman Spectroscopy*, S. Asher and P. Stein (eds), John Wiley & Sons, Pittsburgh, 1996, p. 1072.
165. D.B. Chase, *Mikrochim. Acta*, **14**, 1 (1997).
166. S. Farquharson and S.F. Simpson, *Proc. SPIE*, **1681**, 276 (1992).
167. N. Everall, in: *An Introduction to Laser Spectroscopy*, D.L. Andrews and A.A. Demidov (eds), Plenum Press, New York, 1995.
168. N. Everall, B. King and I. Clegg, *Chem. Britain*, **July**, 40 (2000).
169. A.D. Shaw, N. Kaderbhal, A. Jones, A.M. Woodward, R. Goodacre, J.J. Rowland and D.B. Kell, *Appl. Spectrosc.*, **53**, 1419 (1999).
170. D. Renaut, J.C. Pourny and R. Capitini, *Optics Lett.*, **5**, 233 (1980).
171. W. de Groot and R. Rich, *Proc. SPIE*, **3535**, 32 (1999).
172. W.H. Weber, M. Zanini-Fisher and M.J. Pelletier, *Appl. Spectrosc.*, **51**, 123 (1997).
173. A.S. Gilbert, K.W. Hobbs, A.H. Reeves and P.P. Hobson, *Proc. SPIE*, **2248**, 391 (1994).
174. I.E. Wachs, in: *Handbook of Raman Spectroscopy*, I.R. Lewis and H.G.M. Edwards (eds), Marcel Dekker, New York, 2001.

175. D. Uy, A.E. O'Neill, L. Xu, W.H. Weber and R.W. McCabe, *Appl. Catal. B*, **41**, 269–278 (2003).
176. V. La Parola, G. Deganello, C.R. Tewell and A.M. Venezia, *Appl. Catal. A*, **235**, 171–180 (2002).
177. G.J. Hutchings, J.S.J. Hargreaves, R.W. Joyner and S.H. Taylor, *Studies Surf. Sci. Catal.*, **107**, 41–46 (1997).



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## Chapter 7

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# More Advanced Raman Scattering Techniques

In previous chapters we have introduced the reader to Raman spectroscopy as most spectroscopists and analysts would use it. We have covered the practical application, the theory, some more advanced applications and many examples. However, modern developments in optics are expanding the opportunities for the effective use of Raman scattering through the construction of devices such as portable spectrometers, mapping and imaging stages and devices for the collection of scattering from nanoscale objects. Further, these developments have led to an improvement in the equipment used in specialist laboratories to measure Raman scattering using more advanced techniques. This makes techniques such as time-resolved methods, Raman optical activity and UV Raman scattering more accessible and has led to an increased interest in multi-photon methods. These include hyper Raman scattering, inverse Raman scattering, and various forms of stimulated Raman scattering such as coherent anti-Stokes Raman scattering. The main reason for the increased interest is that the more complex equipment used for these techniques is confined to a few research laboratories and consequently is not generally available. However, modern optics developments which facilitated the increased use of Raman spectroscopy have also made it more practicable to use the more advanced techniques for specific problems where they have significant advantages. Thus, many readers of this text will not have immediate access to the equipment described later in this chapter, but all spectroscopists should be aware of the possibilities for problems which cannot be solved more simply. It is almost impossible to cover all of the possibilities here, but some key examples of techniques which could grow in importance are described briefly, and these and others are reviewed in [1, 2].

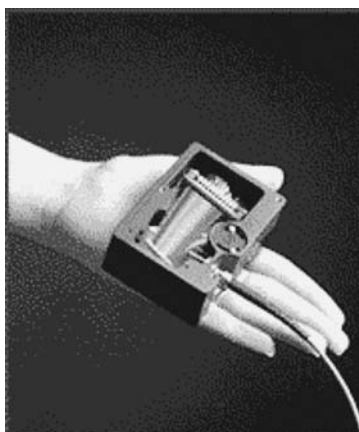
## 7.1 FLEXIBLE OPTICS

The use of optical systems to improve different facets of modern life such as communications, precise measurement, digital photography and video imaging has meant that there is an ever increasing range of high quality optical components available to improve and simplify the construction of spectrometers. These include small diode lasers with an ever expanding range of different frequencies and reasonable lifetimes, good fibre optic technology, better filters such as notch filters, holographic gratings and micro-positioning stages for mapping and sensitive detectors.

There are many obvious examples of the influence this has had. Efficient fibre optic coupling means that the separation of a probe head from the spectrometer is now a commonplace design, as described in Chapter 2. The use of small notch filters instead of monochrometers to remove Rayleigh scattering and specular reflectance has reduced the size of commercial instruments, and the use of inexpensive CCD detectors developed for the video camera has enabled less expensive but effective Raman systems to be built.

As an example of the potential, we mentioned in Chapter 2 that we recently used a laser pointer as an excitation source with an admittedly expensive Raman microprobe system to collect and detect the Raman scattering. This was effective because the microscope focussed the low power of the laser pen onto a small spot increasing the effective excitation power at the sample. However, the signal was broadened due to the fact that the laser beam is not as monochromatic as that from a high quality laser. Since Raman scattering is recorded as a shift from one specific excitation frequency, if the excitation line covers a range of frequencies, each peak in the spectrum due to the Raman scattering will also cover a range of frequencies. Thus, broadening of the peaks occurs even before natural line broadening from the molecular processes is taken into account. Thus, a good monochromatic source is essential for the best results. This means that in high quality Raman systems even some diode lasers which can be bought quite cheaply can become expensive as a source since they require the addition of a temperature-stabilized unit. Further depending on the type of laser, there may also be a requirement for an optical feedback loop to prevent a frequency shift caused by light back-scattered or reflected into the laser.

When a microscope or a fibre optic cable is used in the collection system, the size of the image is small and this enables a small detector to be used. Figure 7.1 illustrates a system designed for the collection of Raman scattering which can be held in the palm of the hand. This spectrometer uses a filter to remove Rayleigh scattering and specular reflectance, and a fibre optic cable to couple the probe to the monochromator and CCD detection system shown. Even simpler systems can be constructed if all that is required is total Raman



**Figure 7.1.** Small fibre optic spectrometer. Reproduced by permission of Ocean optics.

scattering rather than a Raman spectrum. In this case, a diode laser, a notch or edge filter and a simple detector such as an avalanche photodiode can be used.

As an example of the advantages of flexible optics, consider the problem of using Raman scattering in liquid chromatography detection. There would be considerable advantages since Raman detection is molecularly specific and would identify the presence of certain analytes without further labelling. However, the lack of sensitivity of Raman scattering in solution is a severe inhibition. The use of a tightly focussed laser beam as is used in a microscope will increase the density at the sample and compensate to some extent. However, the detection limit is often still too high. In Chapter 5 we discussed the possible use of SERS to improve detection limits. However this is often either not applicable or inconvenient. It is also possible to use Raman scattering with other optical arrangements. For example, the laser beam instead of being launched into a fibre optic can be waveguided through a narrow tube filled with a solution containing the substance to be detected. The materials and dimensions for the construction of these tubes require to be correct for effective waveguiding. When set up correctly, the laser beam can pass through many metres of the sample exciting Raman scattering as it passes. It then exits at the far end of the waveguide along with the associated Raman scattered radiation. This huge path length significantly increases the signal to noise ratio of the Raman scattering.

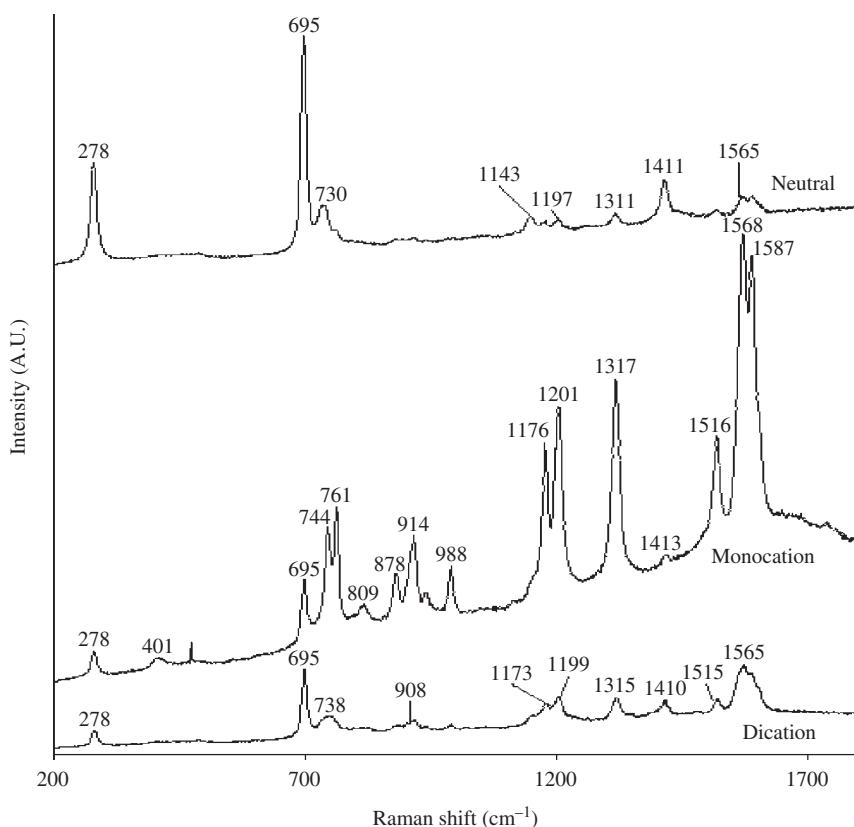
The increased flexibility with fibre optic coupling has led to the combination of Raman spectroscopy with many other techniques. The simplest example does not need a fibre optic coupled head though it can be convenient to use one. Thin layer chromatography (TLC) plates have been examined by Raman spectroscopy to determine the position of spots across the plate. The spots are

easily examined, *in situ*, using a microscope or a fibre optic plate reader. The separated organic analytes are easily distinguished by Raman scattering from the inorganic silicates or other material of the chromatography plate. However, it is often the case that fluorescent stains are used with TLC for detection and this can totally obscure the Raman spectrum. In some cases, this can be turned to advantage using resonance or SERRS.

Many other combined techniques which use either fibre optic coupled Raman probes or modified microscope systems with different chromatographies (HPLC, CE, GPC, FIA and GC) have been reported using both on-line and off-line detection. Raman spectrometers have also been coupled to differential scanning calorimeters (DSCs) to follow changes in the spectrum with temperature and to electrochemical cells to follow changes with voltage. In the latter field, optically transparent thin layer electrodes (OTTLE) are often used in electronic spectroscopy to obtain spectra at controllable potentials. Using the extra enhancement of resonance, it is also possible to follow changes in such cells using Raman spectroscopy. An example of the Raman spectrum of the radicals produced in an OTTLE cell when a charge transfer material, used in the production of light emitting diodes, is dissolved in solution is shown in Figure 7.2 (see also Section 6.6).

The spectra were obtained on a microscope system with a macro-sampler (see Section 2.7) using a cell which had been designed for electronic spectroscopy. However, a similar result was obtained from a fibre optic coupled probe. The use of the same cell enabled the additional molecular specificity of Raman scattering to be used to assist the interpretation of the results obtained with electronic spectroscopy.

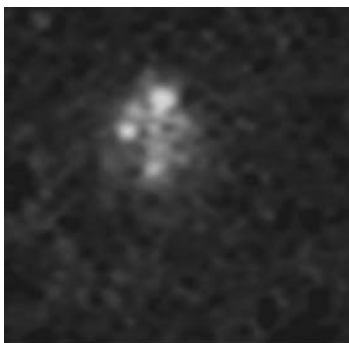
Other examples of the use of flexible optics have been described in earlier chapters and the important techniques of Raman/SNOM, Raman/AFM and Raman/SEM are described later in this chapter. New techniques are appearing regularly. As an example, the use of optical tweezers is an expanding field, largely because the quality and flexibility of modern optics make it simpler. In tweezing, a tightly focussed intense beam of light irradiates a particle. In some particles such as silica particles, the beam passes through the particle and then re-emits. If light enters from the top, the optical path causes repulsive forces to be created at the surface of the particle where the light enters and where it is re-radiated at the foot. The direction of these forces holds the particle in the beam trapping or 'tweezing' it. The trapped particle can then be manipulated by external optics so that it is placed in a suitable position. Raman spectra can be obtained from these particles simply by collecting the scattered light. This system can be set up to give SERS/SERRS by using silver coated particles. However, silver coated particles do not trap well since instead of the light being transmitted through the particle, it is collected by the surface plasmon, moved round the surface of the particle and re-radiated. One method of carrying out SERRS effectively is to lightly coat the particles with silver so that the beam is



**Figure 7.2.** Raman spectra taken from an OTTLE cell containing a solution of a charge transfer agent or the mono- or di-cation. The mono and di-cation spectra are resonant or preresonant increasing their intensity. (Reproduced with permission from R. Littleford, M.A.J. Paterson, P.J. Low, D.R. Tackley, L. Jayes, G. Dent, J.C. Cherryman, B. Braon and W.E. Smith, *Phys. Chem., Chem. Phys.*, **6**, 3257–3263 (2004).)

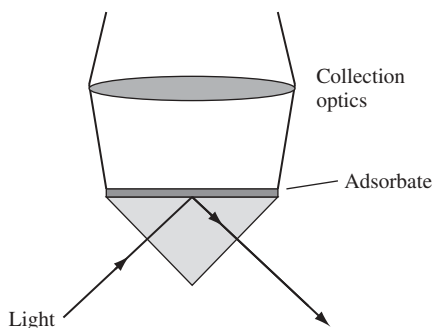
still transmitted but with enough silver on the surface to give SERRS. Figure 7.3 shows SERRS from a lightly coated particle trapped in a tweezer system using 532 nm excitation. The scattering is from points on the particle presumably where the silver is most heavily deposited. One remarkable feature of this is the fact that it can be viewed through a microscope with a standard video camera. This indicates the high sensitivity of SERRS and the consequent ability to detect it with simple equipment. The high power of the tweezing beam can cause ready sample photodegradation and another way to use this system is to use more heavily coated particles which do not trap well and touch the edge of the particle with the beam. This still gives good SERRS but the signal is stable for much longer.





**Figure 7.3.** SERRS from a single silica particle indicating the short lived pulse of Raman scattering.

Another effective method is to use the evanescent field created when a light beam is close to a surface. In one simple arrangement, a prism is set up so that the sample to be analysed is presented as an adsorbate layer on top of a flat surface and the exciting beam is directed at an angle from below. If the angle of the laser beam is such that it is reflected from the surface, the evanescent field created at the surface causes an electric field on the area directly above the surface where the adsorbate is placed. This will cause Raman excitation from the adsorbate. The Raman excitation is then collected from the side away from the prism as shown in Figure 7.4. However, since the beam is reflected and does not directly contact the adsorbate very much, higher laser powers can be used with less interference from non-Raman scattered light. A more sophisticated development of this is to use a quartz crystal in a manner analogous to that used for ATR in infrared scattering (see Section 2.6.3).



**Figure 7.4.** Raman scattering collected using evanescent field excitation.

Thus, the modern spectroscopist has a 'toolkit' of components which enable the construction of instruments designed to meet specific problems. The power of this approach is rapidly increasing. One example of this is the handheld 'white powder detector' used in drug detection and described earlier. Section 7.2 describes more advanced ways in which optics and equipment can be configured to improve the spacial resolution of the system.

## **7.2 TUNEABLE LASERS, FREQUENCY DOUBLING AND PULSED LASERS**

With the exception of one example, all the work described so far can be achieved with continuous wave (CW) lasers which continuously emit light of a specific frequency. However, both tuneable and pulsed lasers can have specific advantages in Raman scattering and are widely available. Much of the physics for the development of these systems is not new, but what is new is that the systems are more reliable and simpler to use than was the case a few years ago.

Some laser systems provide tuneable radiation so that the frequency of the monochromatic beam can be selected by the operator within a specific wavelength range. The standard systems most widely used to achieve this are dye lasers or solid state tuneable lasers. In the dye laser, a powerful monochromatic laser beam from a 'pump' laser is passed through a flowing stream of dye solution. The dye is excited and emission occurs over a range of frequencies. A tuned optical cavity is used to create the laser radiation. One frequency is selected, for example by turning a prism in the cavity so that radiation of only the desired frequency is repeatedly passed back and forward inside the cavity. During this process the pump laser continuously excites molecules into the excited state. A process of stimulated emission now occurs. This process is common to all laser systems. When a photon of light passes a molecule containing an electron in an excited state of exactly the same frequency, emission is stimulated and the two photons emerge with the same energy and in phase. Stimulated emission is a relatively efficient process compared to spontaneous emission and consequently molecules pumped up to the excited state by the pump beam preferentially reradiate with the chosen frequency. This creates an amplified beam in the optical cavity in which all the photons are of one frequency and in phase. The beam continues to oscillate back and forward inside the cavity until a power level is reached at which one of the mirrors is not sufficiently strong to prevent the beam passing through it. The laser emission then exits through this mirror. By simply altering the angle of the prism in the cavity, the operator can change the frequency of laser emission within the region in which the particular dye used is effective. Overall this is an inefficient process with considerable energy being lost, for example from all the light

which was emitted by the dye and not tuned into the cavity, but powerful pump lasers are readily available and consequently an effective system can be purchased or constructed. The main problem with this system is the use of the flowing stream of dye. More recently, solid state systems have been developed which will provide tuneable radiation. They use ion-doped crystals such as titanium in sapphire in place of the dye. Again, the actual process is inefficient but it is a price worth paying if tuneable radiation is required.

Another development which is now readily available is the use of frequency doubled lasers where a powerful laser such as a Nd/YAG system which emits at 1064 nm is used. The laser beam is directed into a crystal which produces second harmonic generation. The beam of light is emitted at double the frequency but with a much lower power. In addition to frequency doubling, frequency tripling and frequency quadrupling are achievable through the same effect. Thus, a Nd/YAG laser which emits at 1064 nm can be used to obtain appreciable laser power at 244 nm in the UV. Further, a powerful argon ion laser can be frequency-quadrupled to get a range of frequencies in the UV. This provides effective long-lifetime UV sources for Raman scattering.

Finally, there is a very large group of lasers which are used in many optics laboratories and which have been neglected so far. Pulsed laser systems are now readily available in anything from large laser form to chip form. For the study of some processes such as very fast events, these lasers are essential. We use a pulse system when discussing the advantage of Kerr-gating in reducing fluorescence later in this chapter. Other examples of the use of pulsed lasers are given below. The frequency at which pulses are emitted varies from the microsecond to the femtosecond and each frequency range has its own unique merits. The peak power in the pulse in these lasers can be very high but is delivered only for a short period of time. Important parameters in the selection of a pulsed laser include the frequency of the radiation, the peak power and the repetition rate (rep rate). High peak power and fast rep rates might seem ideal but what this will do very often is cause photodegradation; a compromise using a lower rep rate and a lower peak power is often more effective in Raman scattering. In some cases, low peak powers and fast rep rates are used simply to mimic a CW laser, particularly when an available pulse source is in a frequency region where a simple CW laser is not available. In general, pulsed systems are widely used where they are deemed to have a specific advantage such as in the study of fast reaction processes. With the highest frequency systems, the effect of Heisenberg's uncertainty principle becomes marked. In spectroscopy terms this can be stated as,

$$\Delta E \cdot \Delta t = h/2\pi$$

When  $\Delta t$  is very short as in a femtosecond system,  $\Delta E$  becomes large making the Raman bands very broad.

### 7.3 SPATIALLY RESOLVED SYSTEMS

A major limitation for most optical techniques is that the smallest sample which can be located and defined requires to be of about the size of the wavelength of the light. It is possible to detect the presence of smaller sized particles but the definition of the image rapidly decreases and even with two-photon techniques, samples less than about 300 nm in diameter cannot be properly defined using visible excitation. However, visible spectroscopies and in particular Raman spectroscopy give considerable molecular information and use lower frequency, less destructive beams than higher frequency techniques such as electron microscopy. As a result, techniques using Raman scattering which can give information from nanoscale samples are of considerable use.

There are simple ways that a good Raman spectrum can be obtained from nanoscale samples. For example, if a particle to be analysed can be isolated and adsorbed on the surface so that no other effective Raman scatterer lies within a few microns of it, Raman scattering can be recorded under a microscope. The sample can then be relocated under a transmission electron microscope (TEM) or scanning electron microscope (SEM) and defined. It has to be recognized that the Raman scattering is measured from only part of the area illuminated by the focussed laser beam. This means that a strong Raman scatterer is more effective here and there can be a problem with increased reflection and scattering from the area of the surface which is irradiated with the focussed radiation but does not contain the sample.

In Chapter 2, Figure 2.19 shows a SERRS map of 30 nm silver particles. The individual Raman signals can be clearly seen with a resolution of 1  $\mu\text{m}$ . However, since all the signals arise from the 30 nm particles, it can be said that the resolution is essentially 30 nm. To locate these particles accurately would require another technique such as TEM/SEM or the use of the atomic force microscope (AFM).

The need to examine structure at a greater resolution than can be obtained optically led to the creation of a combined SEM/Raman system. The Raman beam is introduced into the SEM through a fibre optic probe. It is focussed through a hole in a concave mirror directly onto a sample mounted on the sample stage. The mirror also has a hole to allow the electron beam to contact the sample. The remaining mirror surface is then used to collect a cone of Raman scattering back through the probe for analysis outside the SEM. Figure 7.5 gives a diagram of the equipment. The use of such equipment has considerable potential but care has to be taken with the power of the electron beam. The power often used in a normal thermionic SEM source can destroy organic layers very quickly, so low power settings or a field emission source should be used wherever possible.

Another method that is growing in popularity is the use of scanning near-field optical microscopy (SNOM). In one form of this technique, a glass fibre is



**Figure 7.5.** A combined SEM/Raman system. The Raman spectrometer is integrated into the side of the SEM. (Reproduced with permission from Renishaw plc.)

coated with aluminium or another metal. The fibre is heated and pulled to provide a very narrow metal clad fibre over a short length. It is then cleaved at the narrow part to leave a narrow, optically clear small aperture. When light is launched down the other end of the fibre, it is contained in the fibre by the metal coating. The amplitude of the light is compressed within the tube as it narrows and the light emerges from the narrow aperture. Apertures down to about 50 nm are used. Consequently, if the fibre can be placed almost in contact with the surface, the effective irradiation area of the surface is a 50 nm circle and this is essentially the spatial resolution of the technique. The way in which this is done is usually to adapt the technology developed for AFM. The very small excitation volume means that fewer molecules are excited compared to normal microscopic Raman techniques. In one sense this can be regarded as an improvement in sensitivity. However, the inefficiency of the excitation method and the difficulty of collection from close to the tip mean that long accumulation times are often required. The simplest method to collect the Raman scattering is to arrange collection optics to collect a cone of scattering from the small area excited by the beam emerging from the fibre. There is no need for the collection optics to be focussed down to 50 nm since the area irradiated with the intense light will give the most efficient Raman scattering. There are many other possible arrangements of this type but all have essentially the same advantages and disadvantages. The obvious advantage is in spatial resolution, and the disadvantage is that the process of confining the light is inefficient and there

are compromises with the collection efficiency as well. The result is that this works best with strong Raman scatterers and with long accumulation times. Raman scattering is also generated in the fibre and must be removed with a notch or edge filter to obtain the best results.

In another technique the AFM is combined with SERS/SERRS detection. Here, the cantilever tip of the AFM is coated with silver or gold so that the tip is covered in metal. If the tip contacts the surface and the excitation beam irradiates the area, strong SERS/SERRS can be obtained from the surface. Since this means an enhancement of  $10^6$  or more, it is light from the point where the tip touches the surface that is collected. The AFM map defines the exact position at which the Raman scattering is collected. Thus, the resolution is approximately that of the tip and certainly very small areas can be located and interrogated in this way. Once again, the Raman collection optics are set to collect a cone of scattered light created by the SERS/SERRS from the tip.

There are many variations on the optical arrangements for these techniques and in fact SNOM is also used with a silver coating so that the edge of the SNOM has a roughened silver tip. In this way, 50 nm Raman excitation is passed directly onto an area of the surface which can be contacted by the silver to create SERS/SERRS. The main drawbacks of these techniques are the compromises made in setting up the instruments, the limited number of samples that are suitable and the difficulties in creating effective, reliable and reproducible coated AFM tips.

## 7.4 NONLINEAR RAMAN SPECTROSCOPY

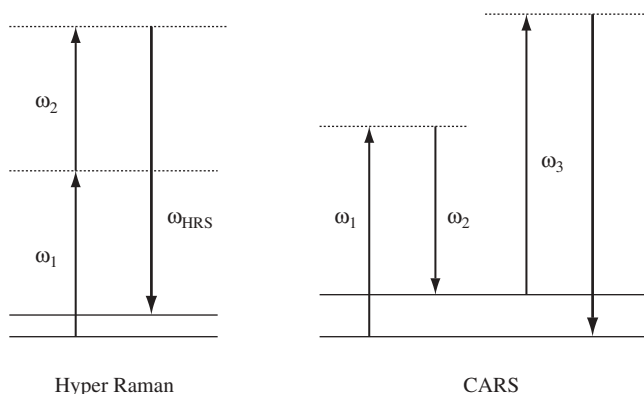
In this book so far, Raman scattering has been described in terms of a single photon event in which the Raman scattering efficiency is linearly related to the laser power. However, what happens at higher power densities if no photo-decomposition occurs? In this case more than one photon may interact with a molecule at the same time causing a multi-photon event, the magnitude of which is not linearly related to the laser power. This condition is easily achieved using the high peak power of the pulses from pulsed lasers. In addition it can be arranged using pulses from one or more lasers to irradiate the sample at the same time. A number of different forms of Raman scattering have been observed by using this approach, and collectively, these are all nonlinear spectroscopies. They have specific advantages for the solution of specific problems. For example, coherent anti-Stokes Raman scattering (CARS) is one way of reducing fluorescence in highly fluorescent media and hyper Raman spectroscopy has selection rules such that asymmetric bands are relatively more intense in the spectrum.

These techniques can add to our understanding of the nature of the molecule but to date, such systems have been expensive and complicated to build.

Recently, advances in optics have made these processes somewhat more accessible, and although still expensive and complex, they are now becoming available to more spectroscopists. In this book, only the outline of a few of these techniques will be given in order to illustrate the potential of this type of technology.

In hyper Raman spectroscopy, an intense beam of radiation is focussed onto the sample. This is usually achieved using a 1064 nm Nd YAG laser. If sufficient power is present, and two photons interact with the one molecule then a virtual state is created at double the frequency of the laser excitation. Raman scattering from this virtual state to an excited vibrational state of the ground state is called hyper Raman scattering. There could be some advantages in this. Firstly, Raman scattering from a 1064 nm laser is too low in frequency to be detected using a CCD camera and usually requires an interferometer and FT spectrometer. For those laboratories equipped only with systems which use CCD detectors, the hyper Raman effect could be, in principle, a useful way of obtaining Raman scattering with this low frequency laser. Besides providing a different spectrum, this will greatly reduce fluorescence. The main disadvantage is that hyper Raman scattering is very weak, and very high laser powers are required to achieve effective scattering. This is usually achieved with pulsed lasers. Such an arrangement is likely to cause an unacceptable amount of heating and sample degradation in many systems. A diagram of the hyper Raman process is given in Figure 7.6.

Perhaps the most widely used nonlinear technique is CARS. Reviews on this technique can be found in [1, 2]. In this technique, a number of laser excitation sources are required. In its most standard form, three different laser sources are used. One beam creates a virtual state as for ordinary Raman scattering. The



**Figure 7.6.** Diagrammatic representation of hyper Raman scattering and CARS.

frequency of the second beam is chosen to have a frequency equal to that which would be scattered in spontaneous Stokes Raman scattering. This stimulates the creation of an excited vibrational state. A third laser is then used to excite the molecule to a second virtual state. Scattering from this second virtual state, which returns the molecule to the ground state, is called CARS. A diagram of this process is shown in Figure 7.6. This effect can be somewhat simplified by using only two lasers. In this case the photons shown as upward ( $\omega_1$  and  $\omega_3$ ) are from the same laser so that  $\omega_1 = \omega_3$ .

Clearly, it is essential for these nonlinear processes that all photons involved are present on the molecule at the same time. This means that the phase matching of the beams involved is critical. This can be done simply by making the beams co-linear but, until recently, in the most common CARS setup, technique in which the beams were arranged at an angle to each other was used. The reason for doing this is that, if the beams are co-linear, the length over which the scattering occurs can be quite long and consequently it can be quite difficult to collect the radiation effectively from a volume containing enough molecules undergoing the CARS process. When the laser beams are set at an angle, the interacting length between the beams is much shorter making collection easier. However, although this works, the phase matching condition is quite complex and difficult to calculate. Angles between the beams of about  $7^\circ$  are typically used. This type of arrangement is known as BOXCARS. It should be noted that unlike ordinary Raman scattering, CARS is emitted in specific directions and has to be detected in these directions.

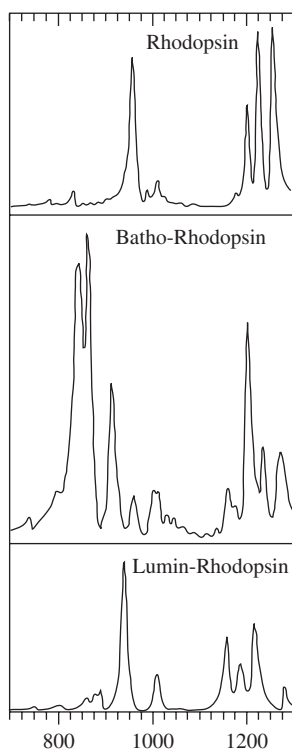
Recently, a considerably simplified version of the CARS system has been developed which makes it more practical. In this, the laser light from two lasers is sent co-linearly and in phase down a microscope. The sharp focus of the microscope removes the difficulty with co-linear beams and still provides sufficiently effective phase matching to obtain effective CARS at the focus. This makes these systems much simpler for the average spectroscopist. In addition, the tuneable laser required to provide the second frequency can be easily obtained in a reliable manner using a modern solid state laser and an optical parametric oscillator (OPO). These systems are still expensive and are limited to research applications, but a significant advance in simplicity has been achieved and it may be that in future, further advances will make the technique more widely available.

The main advantage of CARS is that it is an anti-Stokes process and, as a result, fluorescent-free spectra can be obtained. However, in solution, there is an appreciable background associated with CARS that limits the value of this advantage. Again the selection rules are specific to CARS and if the spectrum is compared to the normal Raman or resonance Raman spectrum, this can give a more effective assessment of the properties of a molecule. One example where CARS has been used is in the analysis of gas mixtures in the head of combustion engines.

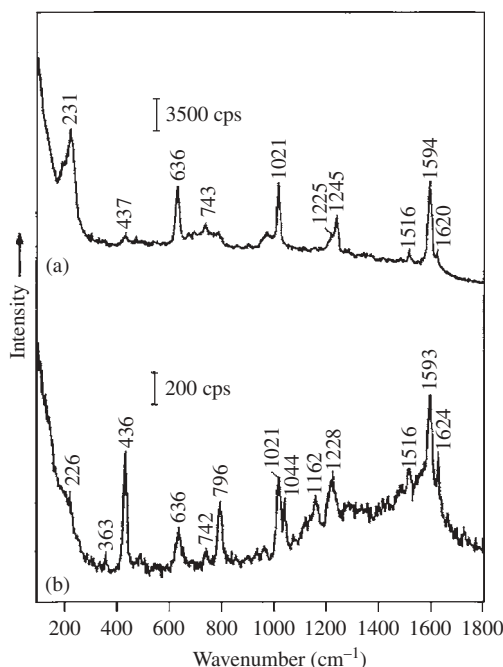


For many solution phase applications, additional CARS intensity is gained by using excitation frequencies so that resonant or pre-resonant conditions are used. The addition of resonance enhancement gives greater CARS and consequently makes it easier to discriminate the signals from the associated background signal. An example of CARS for rhodopsin is shown in Figure 7.7.

Both hyper Raman and CARS are often used with excitation frequencies which are close to that of an electronic transition in the system. This enables a pre-resonant or resonant effect to increase the intensity of the signal. Clearly, SERS will be very effective with these methods as well. Figure 7.8 shows a spectrum of hyper Raman/SERS. The compound chosen here (pyrazine) is one that has often been used to probe the SERS effect. The main advantage is that it has a centre of symmetry and consequently in Raman scattering could give symmetric vibrations with no evidence of any infrared active vibrations in the spectrum. In SERS there are more vibrations since the adsorption to the



**Figure 7.7.** CARS of rhodopsin. (Reproduced with permission from F. Yager, L. Ujj and G.H. Atkinson, *J. Am. Chem. Soc.*, **119**, 12610 (1997).)



**Figure 7.8.** SERS (top) and surface enhanced hyper Raman scattering (foot) of pyrazine. (Reproduced with permission from W.H. Li, X.Y. Li and N.T.U. Yu, *Chem. Phys. Lett.*, **305**, 303 (1999).)

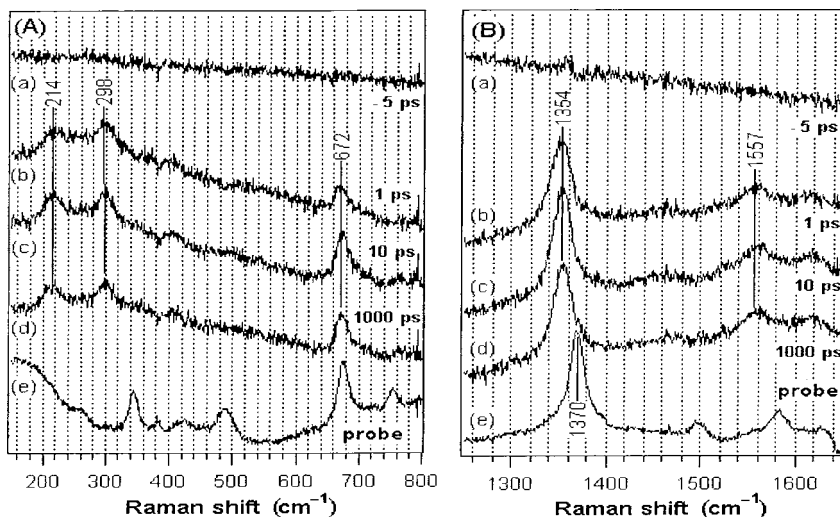
surface breaks the centre of symmetry and makes it possible for infrared active bands to appear. In surface enhanced hyper Raman, even more breakthrough of infrared active modes is observed (see Figure 7.8).

There are many more ways in which pulsed lasers can be combined to achieve nonlinear Raman scattering. Stimulated Raman scattering and inverse Raman scattering are two of the most commonly cited. Stimulated scattering is created by tuning in a second frequency to stimulate the Raman scattering process in a manner analogous to that used to create CARS but using only  $\omega_1$  and  $\omega_2$ . In inverse Raman scattering both the Rayleigh and Raman scattering wavelengths are excited simultaneously. In some cases broadband radiation is used to excite the Raman bands. In the correct circumstances energy transfer within the molecule can lead to absorption at the Raman frequencies rather than scattering, hence the use of the term 'inverse scattering'. However, these techniques are little used and a considerable amount of spectroscopic theory underlies the exact nature of the effects. The *Handbook of Vibrational Spectroscopy* [1] has short articles which would act as a lead-in to further studies in this field.

## 7.5 TIME RESOLVED SCATTERING

With CW lasers, conventional Raman scattering is obtained by collecting photons over a period of time which can extend from seconds to hours, depending on the sample. To obtain evidence on events which occur in the pico- or nanosecond timescales using Raman scattering, a number of strategies are used. One of the most common is to use a pump/probe system. In this arrangement, the output from a pulsed laser is divided into two beams. One is delayed by a chosen number of pico-, nano- or femtoseconds. The pump beam then initiates a process such as a photochemical process in the molecule. The delayed probe beam then interrogates the sample and the Raman scattering resulting is recorded. Obviously, the number of photons scattering for any one pulse is usually quite small. By using a detection system which is synchronized with the laser pulses, an appreciable signal is accumulated over many pulses. One problem with this is that the high peak powers can initiate photodegradation as well as the photochemical reaction desired.

One beautiful example of this approach has been the study of the photodissociation of carbon monoxide bound to the heme in certain enzymes. An example of this effect is shown in Figure 7.9. In this approach, the pump beam is used to cause the initial photodissociation. By selecting different delay times



**Figure 7.9.** The photodissociation of CO from the heme centre in myoglobin. The band at  $1370\text{ cm}^{-1}$  is the oxidation state marker. Dissociation of the CO from the heme causes reduction and other changes. (Reproduced with permission from A. Sato, Y. Sasakura, S. Sugiyama, I. Sagami, T. Shimizu, Y. Mizutani and T. Kitagawa, *J. Biol. Chem.*, **277** (36), 32650–32658, Sep. 6, 2002.)

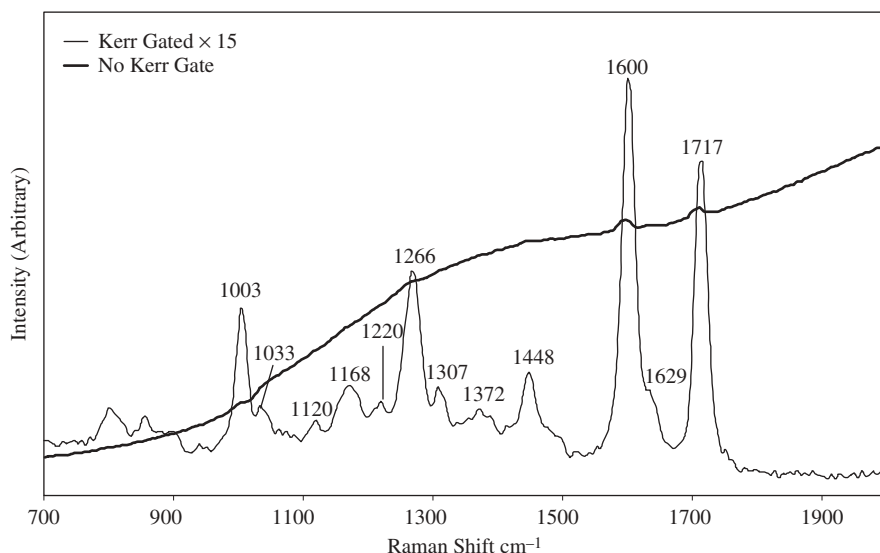
between the pump and the probe, Raman scattering from carbon monoxide, which occurs at different times after band dissociation and therefore at different separation distances between the carbon monoxide and the heme, can be recorded. From this data, good evidence about the pathway of carbon monoxide desorption in the enzyme is obtained. This is only one of many examples of the use of pulse laser sequences.

Usually, pico- or nanosecond pulses are used to allow the photochemical event to occur and the Raman scattering to be collected before the next pulse. With femtosecond lasers, the pulses occur at a faster rate than the vibrational process (in the picosecond range). Thus, a molecule can be excited many times before one vibration takes place and the excitation is faster even than the Raman scattering process. The result is that a ringing effect can be obtained like hitting a bell with a hammer. The interpretation of the complex data obtained from this type of approach lies outside the scope of this book. However, the information which can be obtained for specific problems particularly concerning short lived species is unique. Systems such as haemoglobin and the light-harvesting proteins have been studied.

Another use of pulsed lasers is to overcome fluorescence, a major disadvantage of Raman scattering, by employing a Kerr gate. The method exploits the fact that when a powerful beam of light is passed through a sample, it can cause changes in the dielectric properties of the medium. This effect, the optical Kerr effect, can be set up so that in an effective medium, the plane of polarization of the incident light is rotated by  $90^\circ$  when radiation passes through it.

By splitting the pulse from the laser into two parts, the system can be set up so that the scattered light from one part of the pulse excites the sample at the same time as the Kerr medium is perturbed by the other part of the pulse. Any light passing through it from the sample has the plane of polarization rotated by  $90^\circ$  in the medium. To create a Kerr gate, the scattered radiation from the sample is passed through a polarizer, into the Kerr medium, then through a second polarizer and onto the detector. The two polarizers are set to be at  $90^\circ$  to each other so that no light can pass from the sample to the detector. This is the closed state of the Kerr gate and is the case before the radiation contacts the sample. However, if a sample is excited by one part of the pulse and the second part passes through the Kerr medium, it will rotate the plane of polarization of the scattered light by  $90^\circ$  so that radiation can pass through the analyser and be detected. This is the open gate. The length of time the gate is open is defined by the shaping of the second part of the pulse so that it arrives slightly later than the scattered light and ends a pre-decided amount of time later.

If Raman scattering and fluorescence are both produced from the sample, no signal will be detected before the Kerr gate is opened by the pulse reaching the Kerr medium or after it is closed by the pulse leaving it. Since Raman scattering is faster than fluorescence in many but not all cases, it is possible to set this system up so that it collects only the first few picoseconds of emission following

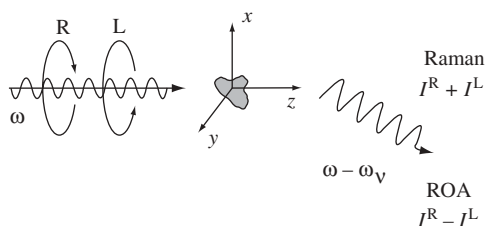


**Figure 7.10.** Kerr gated (light line) and normal Raman scattering (heavy line) for a fluorescent street sample of cocaine. (Reproduced with permission from R.E. Littleford, P. Matousek, M. Towrie, A.W. Parker, G. Dent, R.J. Lacey and W.E. Smith, *Analyst*, **129**, 505–506 (2004).)

the pulse. This is predominantly Raman scattering. In this way, efficient fluorescence rejection is obtained every time a pulse of light irradiates the sample. These pulses are accumulated over a period of time. Figure 7.10 shows the emission spectrum from a street sample of cocaine, which normally fluoresces, with and without the Kerr gate. The sharp Raman spectrum obtained with the Kerr gate is quite clear. In this case, it is the spectrum of a 75% sample of cocaine. However, some of the weaker bands are actually due to impurities present in the sample which also give effective Raman scattering. These can be separated by considering the energies and intensities of the normal pure cocaine Raman spectrum.

## 7.6 RAMAN OPTICAL ACTIVITY

Earlier in this book we discussed mainly the use of CW lasers to produce the excitation beam for Raman scattering. The light used was linearly or plane polarized. However, circularly polarized light can also be used to obtain Raman scattering for molecules that contain a chiral centre. A beam of plane polarized light generated by a laser and a polarizer is passed through a device such as a photoelastic modulator to create circularly polarized light. This

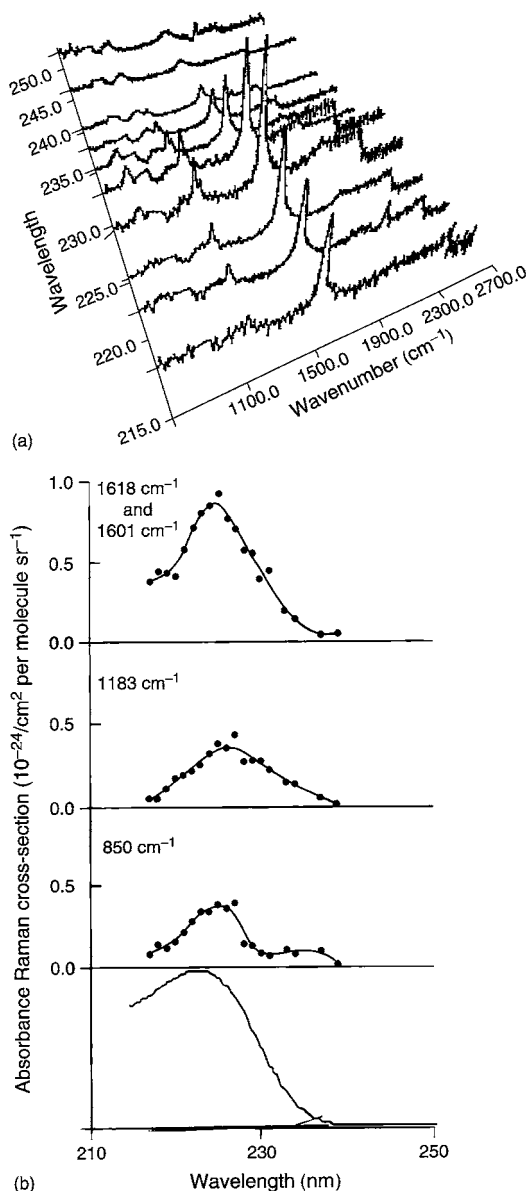


**Figure 7.11.** Schematic diagram of the basic ROA experiment which measures a small difference in the intensity of Raman scattering from chiral molecules in right ( $I^R$ ) and left ( $I^L$ ) circularly polarized light. Incident photons have angular frequency  $\omega$  and Raman scattered photons have angular frequency  $\omega - \omega_v$ . The conventional Raman intensity is given by the sum  $I^R + I^L$  and the ROA intensity by the difference  $I^R - I^L$ . For achiral molecules the ROA intensity is zero. Reproduced with permission from E Blanch (UMIST). (Diagram supplied and drawn by Ewan Blanch at UMIST.)

consists of a block of quartz cut at a particular angle so that when linearly polarized light is passed through it and the block is put under stress, the plane of polarization of the light is rotated. The quartz is held by two clamps which oscillate in such a way that a beam is created which alternates between left circularly polarized (lcp) and right circularly polarized (rcp) light. When this light interacts with a chiral molecule, more scattering will occur from either the lcp or rcp beam depending on which fits with the helix which can be traced on the chiral molecule. The difference in intensity between these beams is Raman optical activity (ROA). The selection rules are more complex because the equations used to predict it involve both the electric and magnetic dipole operators. Until recently the very weak signals obtained and the requirement to retain the circular polarization of the beam have made it difficult to exploit the method. However, advances in optics have made it possible for a commercial instrument to be constructed and good spectra can now be obtained in short periods of time. This technique is proving very effective in that not only does it provide information on chirality within amino acids and polypeptides, it will also selectively identify particular features within a protein such as the degree of folding occurring within it. Further, in addition to advances considered earlier for Raman spectroscopy in general, the use of fast effective modulators to achieve this circular polarization has been a key development. A diagram of the technique is shown in Figure 7.11.

## 7.7 UV EXCITATION

The fourth power nature of the scattering makes UV Raman scattering much more sensitive than visible Raman scattering. Further, the UV region contains



**Figure 7.12.** UV-resonance Raman scattering for tryptophans. Top: Actual spectra with different excitation wavelengths. Foot: Intensity dependence on excitation wavelength of individual peaks. (Reproduced with permission from M. Ludwig, S.A. Asher, *J. Am. Chem. Soc.*, **110**, 1005–1011 (1988).)

many naturally occurring chromophores in a range of molecules. Thus, UV resonance Raman scattering can be obtained from a larger range of species without the use of a label. Fluorescence is no longer a problem at this very short wavelength. In most systems, there are enough vibronic states for the energy to be dissipated into the material and even if it is emitted for some reason, the emission is well outside the region used for Raman detection. There is a drawback, however, in that the high energy radiation and the presence of many chromophores make photodecomposition an even more serious issue than with visible excitation. Samples are often spun or presented to the instrument in a flowing cell to reduce this problem (see Chapter 2). Using part of the advantage gained from the increased efficiency to use a lower excitation power can also reduce the problem. UV Raman scattering has some unique advantages particularly for biological systems. With the correct conditions and laser frequency, it is possible to obtain molecular resonance from groups such as tryptophans and tyrosines present within a protein. The additional resonance enhancement means that vibrations from the resonant groups can be selectively picked out. Figure 7.12 shows the effect of changing excitation with wavelength for tryptophans. For proteins, the resonance effect can be used to select a specific group. For example, by using a resonant frequency for tryptophans, they can be picked up selectively in proteins such as myoglobin. Changing the pH alters the conformation of the protein. The tryptophans are present in a helix within the protein structure and as the helix opens, the intensity of the bands change.

As the frequency of excitation in the UV is increased, a bigger challenge is created from an equipment point of view. In particular the optics have to be of very high quality. Recently, excitation at 209 nm has been used to obtain resonance Raman spectra from the peptide bond. This work has led to Raman scattering being used to give very specific information on protein structure in an elegant way, which could expand as the quality of inexpensive and simple UV lasers and optics improves.

## 7.8 CONCLUSIONS

The above techniques are only illustrative of a very much wider range now available in the literature. Optics developments have resulted in a more widespread use of Raman scattering. Examples include portable Raman spectrometers which can be used outside the laboratory, Raman detectors coupled to other instruments and the use of Raman scattering in hostile environments. The Raman spectroscopist has to decide on the nature of the problem faced before deciding whether the more sophisticated techniques outlined later in the chapter are of value. For many problems, Raman scattering using conventional Raman spectroscopy with either visible or infrared excitation will be the simplest choice. If a more advanced technique is required, there is currently a difficulty



in that some of the equipment is available only in leading research laboratories and often requires an expert to operate it. However, the worlds of nanotechnology and biotechnology in particular may well create specific needs for the use of the more advanced forms of Raman scattering, and this in turn should lead to wider availability. One technique for which this has recently happened in ROA and CARS microscopes are also becoming more common.

## REFERENCES

1. J. Chalmers and P. Griffiths (eds), *Handbook of Vibrational Spectroscopy*, Vols 1 and 2, John Wiley & Sons, Inc., New York, 2001.
2. J.R. Ferraro and K. Nakamoto, *Introductory Raman Spectroscopy*, Academic Press, San Diego, 1994.

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5ª edición

# Química Orgánica



PEARSON  
Prentice  
Hall

L. C. Wade, Jr.

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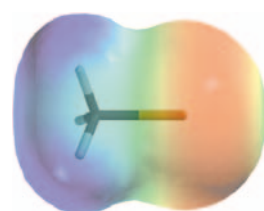
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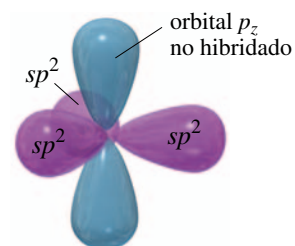


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átomo de carbono con hibridación  $sp^2$  (vista lateral)

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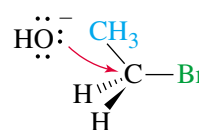
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bromuro de etilo ( $1^\circ$ )  
el ataque es fácil





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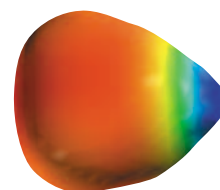
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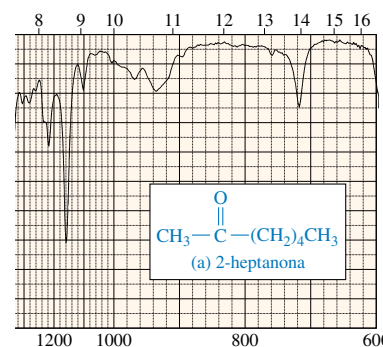
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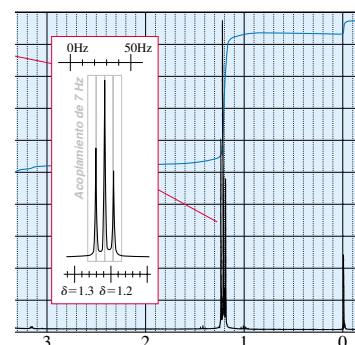
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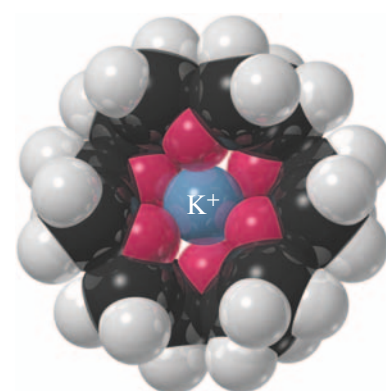
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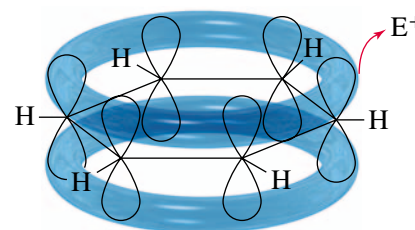
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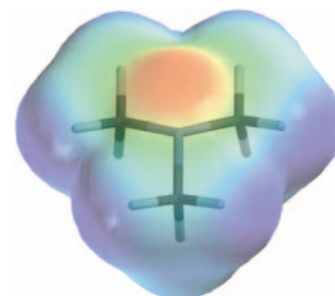
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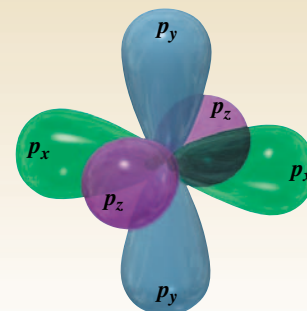
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# CAPÍTULO 1

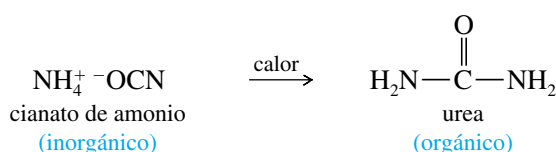
## Introducción y revisión



La definición moderna de **química orgánica** es la *química de los compuestos de carbono*. ¿Qué tiene de especial el carbono que hay una rama de la química que se dedica a él? Al contrario que otros elementos, el carbono forma enlaces fuertes con otros átomos de carbono y con una gran variedad de otros elementos. Las cadenas y anillos de átomos de carbono son tan variadas que se puede formar una variedad interminable de moléculas. Esta diversidad de los compuestos de carbono es la base para la vida en la Tierra. Los seres vivos están formados de compuestos orgánicos complejos con funciones estructurales, químicas o genéticas.

El término **orgánico** literalmente significa «derivado de los organismos vivos». Originalmente, la ciencia de la química orgánica era el estudio de los compuestos que se extraían de los organismos vivos o productos naturales. Compuestos tales como azúcar, urea, levadura, ceras y aceites vegetales eran considerados «orgánicos» y se aceptó el **Vitalismo** como teoría que explicaba su origen: la creencia en que los productos naturales necesitaban una «fuerza vital» para ser creados. Por tanto, la química orgánica era el estudio de los compuestos que tenían esa fuerza vital. La química inorgánica era el estudio de los gases, rocas, minerales y de los compuestos que se podían obtener a partir de ellos.

En el siglo XIX, la experimentación demostró que los compuestos orgánicos se podían sintetizar a partir de compuestos inorgánicos. En 1828, el químico alemán Friedrich Wöhler convirtió el cianato de amonio, obtenido a partir de amoníaco y ácido ciánico, en urea simplemente calentando el cianato en ausencia de oxígeno.



La urea también proviene de los seres vivos y se creía que contenía la fuerza vital, a pesar de que el cianato de amonio es inorgánico y por tanto, según aquella creencia, no poseía la fuerza vital. Algunos químicos sostenían que esa fuerza vital provenía de las manos de Wöhler, pero la mayoría reconocieron la posibilidad de sintetizar compuestos orgánicos a partir de compuestos inorgánicos. También se llevaron a cabo otras síntesis, por lo que la teoría de la fuerza vital se descartó.

Desde que el Vitalismo se descartó a comienzos del siglo XIX, se podría pensar que esta idea habría ya desaparecido, pero estaríamos equivocados, ya que el Vitalismo hoy forma parte de la mentalidad de las personas que creen que los productos «naturales» (derivados de las plantas) son diferentes y más saludables que aquellos compuestos exactamente iguales, «artificiales», que han sido sintetizados.

Como químicos, sabemos que los compuestos derivados de las plantas y los compuestos sintetizados son idénticos. La única diferencia es el contenido en  $^{14}\text{C}$ : los compuestos sintetizados a partir de derivados del petróleo tienen menor contenido del isótopo radioactivo  $^{14}\text{C}$ ,

### 1.1

## Los orígenes de la química orgánica



El corazón artificial Jarvik 7 está compuesto en gran parte de materiales orgánicos sintéticos.

ya que este isótopo ha ido desapareciendo con el tiempo. Los compuestos derivados de las plantas, al haber sido sintetizados recientemente a partir del  $\text{CO}_2$  del aire, tienen un contenido más elevado en  $^{14}\text{C}$ . Algunos suministradores importantes de productos químicos dan los análisis de los isótopos para confirmar que los «productos naturales» que distribuyen tienen mayor contenido en  $^{14}\text{C}$  y son derivados de las plantas. Estos sofisticados análisis dan un aspecto de alta tecnología al Vitalismo del siglo XXI.

A pesar de que los compuestos orgánicos no necesitan una fuerza vital, todavía se diferencian de los compuestos inorgánicos. La característica que distingue a los compuestos orgánicos es que *todos* contienen uno o más átomos de carbono. Pero no todos los compuestos que contienen carbono son orgánicos, sustancias tales como: diamante, grafito, dióxido de carbono, cianato de amonio y carbonato de sodio son compuestos derivados de minerales, y tienen propiedades características de los compuestos inorgánicos. No obstante, la mayoría de los millones de compuestos que contienen carbono se clasifican como orgánicos.

Nosotros mismos estamos compuestos en gran parte por moléculas orgánicas y nos alimentamos de compuestos orgánicos. Las proteínas de nuestra piel, los lípidos de las membranas de nuestras células, el glucógeno de nuestro hígado y el DNA del núcleo de nuestras células son compuestos orgánicos. Nuestros cuerpos también están regulados y son defendidos por compuestos orgánicos complejos.

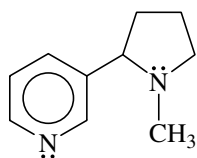
Los químicos han aprendido a diseñar y sintetizar muchas de estas moléculas complejas. Los productos sintéticos se utilizan como productos farmacéuticos, plásticos, pesticidas, pinturas y fibras. La mayoría de los avances más importantes en medicina se debe actualmente a los avances en química orgánica. Así, se sintetizan nuevos productos farmacéuticos para combatir enfermedades y se obtienen nuevos polímeros para elaborar dispositivos ortopédicos con los que sustituir órganos dañados. La química orgánica ha cerrado el ciclo, comenzó con el estudio de los compuestos derivados de «órganos» y ahora nos proporciona los productos farmacéuticos y materiales que necesitamos para salvar o reemplazar esos órganos.

Uno de los efectos de la nicotina es incrementar la concentración de una sustancia química en el sistema de estímulos cerebrales. La liberación de esta sustancia química hace que los fumadores se sientan bien y refuerza la necesidad de fumar.

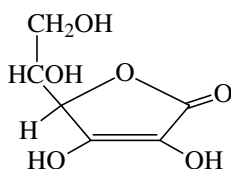
Una de las razones por las que los químicos sintetizan derivados de compuestos orgánicos complejos como la morfina es descubrir nuevas sustancias que mantengan sus propiedades útiles (analgésia) pero no las propiedades indeseables (adicción).



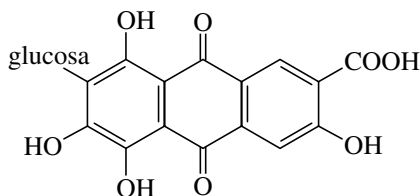
nicotina



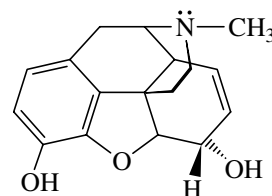
vitamina C



carmín



morfina



A continuación daré cuatro ejemplos de compuestos orgánicos aislados de organismos vivos: el tabaco contiene nicotina, un alcaloide que crea adicción; los escaramujos contienen vitamina C, esencial para prevenir el escorbuto; el carmín proviene de las cochinillas, insectos que suelen estar en las chumberas, y las adormideras contienen morfina, sustancia que mitiga el dolor pero provoca adicción.

Antes de comenzar el estudio de la química orgánica, se han de revisar algunos principios básicos. Muchos de los conceptos de estructura atómica y molecular son cruciales para entender la estructura y el enlace de los compuestos orgánicos.

### 1.2A Estructura del átomo

Los átomos están formados por protones, neutrones y electrones. Los protones están cargados positivamente y se encuentran, junto con los neutrones (sin carga), en el núcleo. Los electrones contienen una carga negativa de la misma magnitud que la carga positiva de los protones y se encuentran en el espacio que rodea al núcleo (Figura 1.1). Los protones y los neutrones tienen una masa parecida, aproximadamente unas 1800 veces la masa de un electrón. A pesar de que prácticamente toda la masa del átomo está concentrada en el núcleo, son los electrones los que participan en los enlaces químicos y en las reacciones.

Cada elemento se caracteriza por el número de protones que tiene en el núcleo (número atómico). El número de neutrones normalmente es parecido al número de protones, pero este número de neutrones puede variar. Los átomos que tienen el mismo número de protones pero diferente número de neutrones se llaman **isótopos**. Por ejemplo, el átomo de carbono más común es el que tiene seis protones y seis neutrones en el núcleo; su número másico (suma de protones y de neutrones) es 12, por lo que lo escribimos con el símbolo  $^{12}\text{C}$ . Aproximadamente el 1% de los átomos de carbono tienen 7 neutrones y su número másico es 13, simbolizado por  $^{13}\text{C}$ . Una fracción muy pequeña de átomos de carbono tiene ocho neutrones, por lo que su número másico es 14. El  $^{14}\text{C}$  es un isótopo radioactivo, con un periodo de semidesintegración (tiempo que tarda una determinada masa de ese isótopo en desintegrarse y perder la mitad de su masa) de 5 730 años. Este tiempo de desintegración del  $^{14}\text{C}$  se utiliza para determinar la edad de los materiales orgánicos de hasta unos 50 000 años de antigüedad.

### 1.2B Estructura electrónica del átomo

Las propiedades químicas de un elemento se determinan por el número de protones de su núcleo y el correspondiente número de electrones que hay alrededor del núcleo. Los electrones forman enlaces y determinan la estructura de las moléculas resultantes. Debido a que los electrones son muy pequeños y están en movimiento, se comportan simultáneamente como partículas y como ondas.

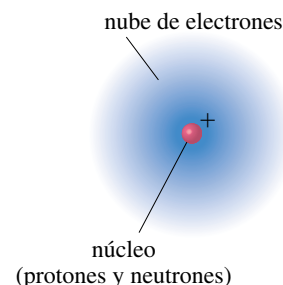
Los electrones que se encuentran moviéndose alrededor del núcleo se encuentran en **orbitales**. El principio de incertidumbre de Heisenberg dice que nunca se puede determinar con exactitud dónde se encuentra el electrón; sin embargo, se puede determinar la **densidad electrónica**, la probabilidad de encontrar al electrón en una determinada zona del orbital. Por tanto, un orbital es un estado de energía permitido para un electrón, con una función de probabilidad asociada que define la distribución de la densidad electrónica en el espacio.

Los orbitales atómicos se agrupan en «capas» o niveles diferentes a distintas distancias del núcleo. Cada capa se identifica por un número cuántico principal  $n$ , siendo  $n = 1$  para la capa de menor energía (la que está más próxima al núcleo). Al aumentar  $n$ , las capas están más alejadas del núcleo, tienen una energía más alta y pueden contener más electrones. La mayoría de los elementos más comunes de los compuestos orgánicos se encuentran en las dos primeras filas (periodos) de la tabla periódica, lo que indica que sus electrones se encuentran en las dos primeras capas de electrones. La primera capa ( $n = 1$ ) puede alojar dos electrones y la segunda capa ( $n = 2$ ) puede alojar ocho.

La primera capa de electrones contiene solamente el orbital  $1s$ . Todos los orbitales  $s$  tienen simetría esférica, lo cual quiere decir que son no direccionales. La densidad electrónica del orbital  $1s$  se representa en la Figura 1.2. Se puede observar que la densidad electrónica es más alta en las proximidades del núcleo y va disminuyendo exponencialmente según va aumentando la distancia al núcleo. Se podría comparar el orbital  $1s$  con una cápsula de algodón, donde la semilla representaría el núcleo. La densidad del algodón es mayor en los lugares próximos a la semilla y su densidad va disminuyendo según se va alejando del núcleo.

La segunda capa de electrones consta de orbitales  $2s$  y  $2p$ . El orbital  $2s$  posee simetría esférica igual que el  $1s$ , pero su densidad electrónica no es una simple función exponencial. El orbital  $2s$  tiene una densidad electrónica más pequeña en las proximidades del

## 1.2 Principios de la estructura atómica



▲ Figura 1.1

El átomo tiene un denso núcleo, cargado positivamente, rodeado de una nube de electrones.

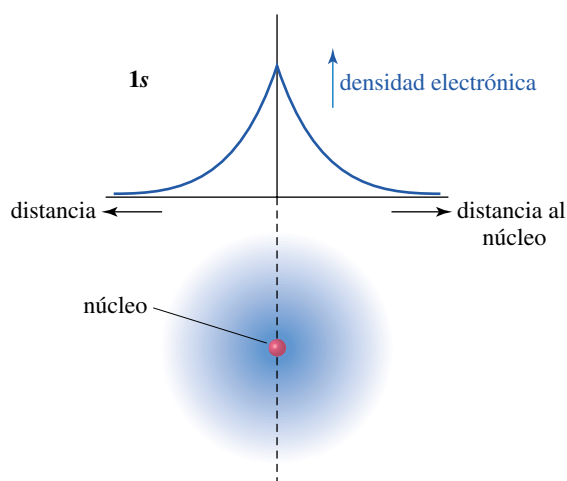
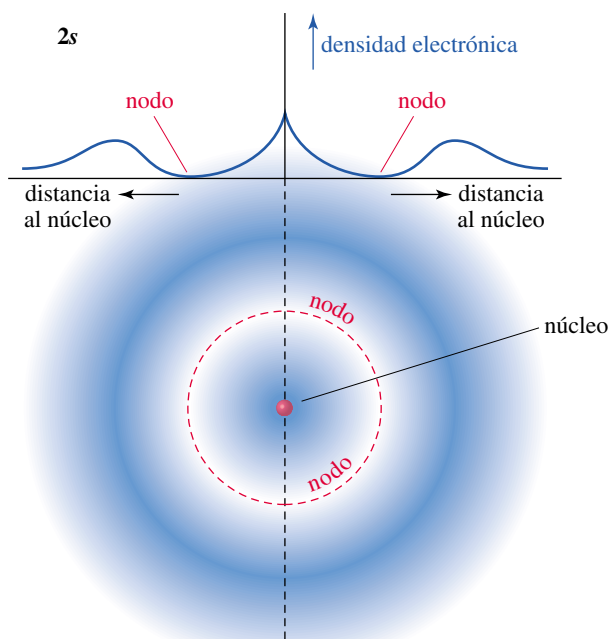
► **Figura 1.2**

Gráfico y diagrama del orbital atómico 1s. La densidad electrónica es más alta cerca del núcleo y disminuye exponencialmente al aumentar la distancia al núcleo en cualquier dirección.

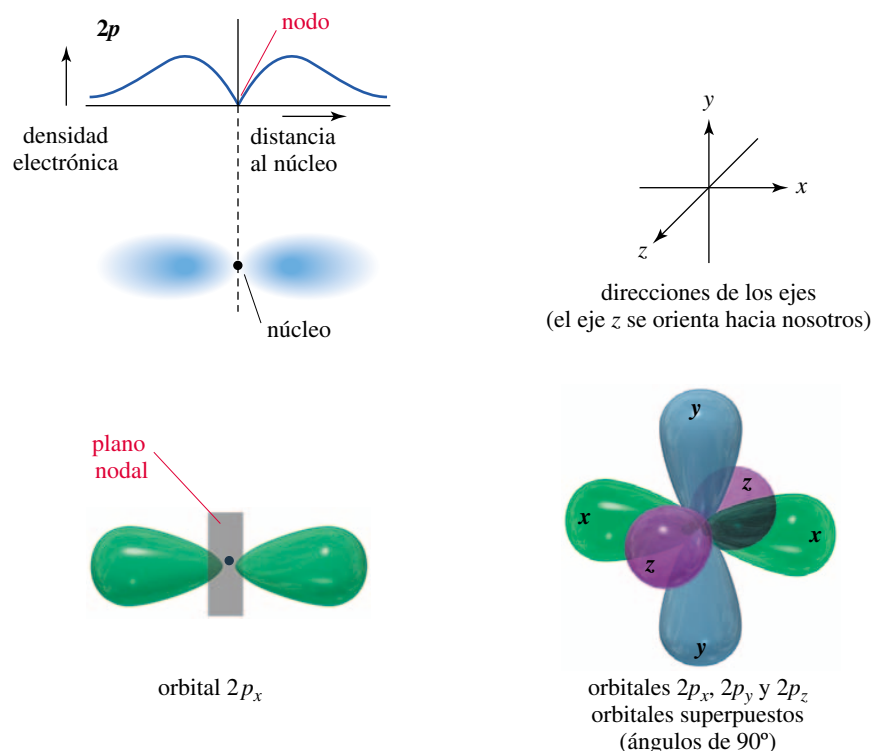
núcleo, ya que la mayor parte de la densidad electrónica está más alejada, más allá de una zona de densidad electrónica nula llamada **nodo**. Como la densidad electrónica del orbital 2s cerca del núcleo es menor que en el caso del orbital 1s, el orbital 2s tiene energía más alta. La Figura 1.3 muestra una representación gráfica del orbital 2s.

Además del orbital 2s, la segunda capa también contiene tres orbitales atómicos 2p, orientados cada uno de ellos en las tres direcciones del espacio. Estos tres orbitales reciben el nombre  $2p_x$ ,  $2p_y$  y  $2p_z$ , según su orientación a lo largo de los ejes  $x$ ,  $y$  o  $z$ . Los orbitales 2p tienen una energía ligeramente superior a la de los orbitales 2s, debido a que la localización media de los electrones en los orbitales 2p se sitúa a una distancia más alejada del núcleo. Cada orbital  $p$  consta de dos lóbulos, uno a cada lado del núcleo, con un **plano nodal** en el núcleo. El plano nodal es una región (plana) del espacio que incluye el núcleo y tiene una densidad electrónica nula. Los tres orbitales 2p únicamente difieren en sus orientaciones espaciales, por lo que tienen la misma energía. Los orbitales que tienen la misma cantidad de energía reciben el nombre de **orbitales degenerados**. La Figura 1.4 muestra las formas de los tres orbitales atómicos 2p degenerados.

► **Figura 1.3**

Los orbitales 2s tienen una pequeña región de densidad electrónica elevada próxima al núcleo, pero la mayor parte de la densidad electrónica está alejada del núcleo, más allá del nodo o región de densidad electrónica cero.





◀ **Figura 1.4**

Orbitales  $2p$ . Hay tres orbitales  $2p$ , orientados unos con respecto a los otros perpendicularmente. Se nombran según su orientación a lo largo del eje  $x$ ,  $y$  o  $z$ .

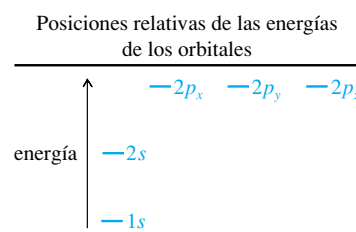
El *principio de exclusión de Pauli* dice que un orbital como máximo puede alojar dos electrones, de forma que sus espines estén apareados. La primera capa (un orbital  $1s$ ) puede alojar dos electrones. La segunda capa (un orbital  $2s$  y tres orbitales  $2p$ ) puede alojar ocho electrones y la tercera capa (un orbital  $3s$ , tres orbitales  $3p$  y cinco orbitales  $3d$ ) puede alojar 18 electrones.

## 1.2C Configuraciones electrónicas de los átomos

*Aufbau* significa «construir» en alemán, y el *principio de aufbau* explica cómo establecer la configuración electrónica de un átomo en su estado fundamental (el de mayor estabilidad). Se comienza con el orbital de energía más baja y se van llenando ordenadamente de menor a mayor energía hasta que se han colocado todos los electrones. La Tabla 1.1 muestra las configuraciones electrónicas en estado fundamental de todos los elementos que forman parte de los dos primeros periodos de la tabla periódica.

**TABLA 1.1** Configuraciones electrónicas de los elementos del primer y segundo periodo

Elemento	Configuración	Electrones de valencia
H	$1s^1$	1
He	$1s^2$	2
Li	$1s^2 2s^1$	1
Be	$1s^2 2s^2$	2
B	$1s^2 2s^2 2p_x^1$	3
C	$1s^2 2s^2 2p_x^1 2p_y^1$	4
N	$1s^2 2s^2 2p_x^1 2p_y^1 2p_z^1$	5
O	$1s^2 2s^2 2p_x^2 2p_y^1 2p_z^1$	6
F	$1s^2 2s^2 2p_x^2 2p_y^2 2p_z^1$	7
Ne	$1s^2 2s^2 2p_x^2 2p_y^2 2p_z^2$	8



► **Figura 1.5**

Primeras tres filas de la tabla periódica. La organización de la tabla periódica se debe al alojamiento de los electrones en los orbitales por orden creciente de energía. Para estos elementos representativos, el número de la columna corresponde al número de electrones de valencia.

**El carbonato de litio, una sal de litio, es un antidepresivo que se utiliza para tratar el problema psiquiátrico conocido como manía. La manía está caracterizada por comportamientos tales como alteraciones del humor, sentimientos de grandeza, obsesiones y dificultad para dormir. No se sabe cómo actúa el carbonato de litio cuando estabiliza el humor de este tipo de pacientes.**

Detalle de la tabla periódica

IA							gases nobles (VIII)
H	IIA	IIIA	IVA	VA	VIA	VIIA	He
Li	Be	B	C	N	O	F	Ne
Na	Mg	Al	Si	P	S	Cl	Ar

En la Tabla 1.1 se ilustran dos conceptos adicionales. Los **electrones de valencia** son los electrones que se encuentran en la capa más externa. El carbono tiene cuatro electrones de valencia, el nitrógeno cinco y el oxígeno seis. El helio tiene dos electrones de valencia y el neón tiene ocho, lo que corresponde, respectivamente, a la primera capa de valencia y a la segunda capa de valencia llenas. En general (para los elementos representativos), la columna o número de grupo de la tabla periódica corresponde al número de electrones de valencia (Figura 1.5). El hidrógeno y el litio tienen un electrón de valencia y los dos se encuentran en la primera columna (grupo IA) de la tabla periódica. El carbono tiene cuatro electrones de valencia y está en el grupo IVA de la tabla periódica.

Observad en la Tabla 1.1 que los electrones de valencia tercero y cuarto del carbono no están apareados, ocupan orbitales separados. A pesar de que el principio de exclusión de Pauli dice que dos electrones pueden ocupar el mismo orbital, los electrones se repelen uno a otro, y el apareamiento requiere energía adicional. La **regla de Hund** afirma que cuando hay dos o más orbitales de la misma energía, los electrones preferentemente se alojan en orbitales *diferentes* antes que aparearse en un mismo orbital. El primer electrón  $2p$  (caso del boro) se coloca en un orbital  $2p$ , el segundo (caso del carbono) en un orbital diferente y el tercero (caso del nitrógeno) se coloca en el último orbital  $2p$ . El cuarto, quinto y sexto electrón  $2p$  se aparearán, respectivamente, con los tres primeros electrones.

**PROBLEMA 1.1**

Escriba las configuraciones electrónicas de los elementos de la tercera fila que se muestra en la tabla periódica parcial de la Figura 1.5

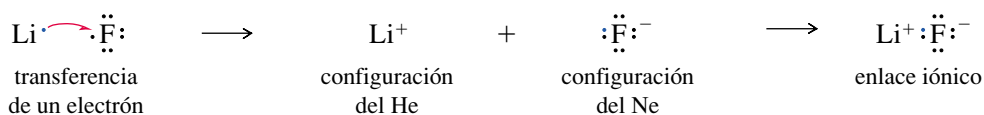
## 1.3

### La formación del enlace: la regla del octeto

En 1915, G. N. Lewis propuso varias teorías nuevas para describir cómo se enlazaban los átomos unos a otros para formar moléculas. Una de esas teorías afirma que una capa llena de electrones es especialmente estable y que *los átomos transfieren o comparten electrones para que de esa forma las capas se llenen de electrones*. Una capa llena de electrones tiene la configuración de un gas noble como el He, Ne o Ar. A este principio se le dio el nombre de la **regla del octeto** porque una capa llena implica ocho electrones de valencia para los elementos de la segunda fila de la tabla periódica.

**1.3A Enlace iónico**

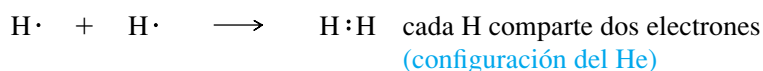
Hay dos formas en las que los átomos pueden interactuar para adquirir configuraciones de gas noble. Algunas veces los átomos adquieren configuraciones de gas noble transfiriendo electrones de un átomo a otro. Por ejemplo, el litio tiene un electrón más en su configuración que el helio, y el fluor tiene un electrón menos que la configuración del neón; el litio pierde fácilmente sus electrones de valencia y el fluor los gana fácilmente:



La transferencia de un electrón da a cada uno de los elementos la configuración de gas noble. Los iones resultantes tienen cargas opuestas y se atraen uno a otro formando un **enlace iónico**. El enlace iónico normalmente da lugar a la formación de grandes estructuras cristalinas en vez de moléculas individuales. El enlace iónico es muy frecuente en los compuestos inorgánicos, pero bastante inusual en los orgánicos.

### 1.3B Enlace covalente

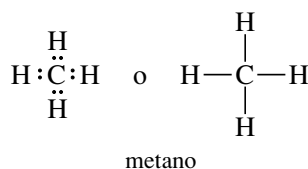
El **enlace covalente**, en el que se comparten electrones en lugar de transferirse, es la forma más habitual de enlace en los compuestos orgánicos. El hidrógeno, por ejemplo, necesita un segundo electrón para conseguir la configuración del gas noble helio. Si dos átomos de hidrógeno se unen y forman un enlace, «comparten» sus dos electrones y cada átomo tiene dos electrones en su capa de valencia.



El enlace covalente se estudiará con más detalle en el Capítulo 2.

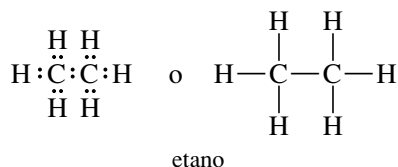
Una forma de simbolizar el enlace en una molécula covalente consiste en usar **estructuras de Lewis**. En una estructura de Lewis cada electrón de valencia se simboliza por un punto. Un par de electrones de enlace se simboliza por un par de puntos o por una línea (—). Se ha de intentar que todos los átomos tengan sus propias configuraciones de gas noble: dos electrones en el caso del hidrógeno y octetos para los elementos de la segunda fila de la tabla periódica.

Considere, por ejemplo, la estructura de Lewis del metano ( $\text{CH}_4$ ):



El carbono contribuye con cuatro electrones de valencia y cada hidrógeno aporta uno, dando un total de ocho electrones. Todos estos ocho electrones rodean al carbono dando lugar a un octeto y cada átomo de hidrógeno comparte dos de los electrones.

La estructura de Lewis para el etano ( $\text{C}_2\text{H}_6$ ) es más compleja:



Una vez más, se han colocado los electrones de valencia (14) y se han distribuido de forma que cada átomo de carbono quede rodeado por ocho electrones y cada hidrógeno por dos. La única estructura posible para el etano es la que se ha mostrado anteriormente, con los dos átomos de carbono compartiendo un par de electrones y cada átomo de hidrógeno compartiendo dos con uno de los carbonos. La estructura del etano muestra las características más importantes del carbono (su habilidad para formar enlaces fuertes carbono-carbono).

Los electrones de la capa de valencia que *no* son compartidos entre dos átomos reciben el nombre de **electrones no enlazantes**. Un par de electrones no enlazantes a menudo también es conocido como un **par solitario**. Los átomos de oxígeno, de nitrógeno y los halógenos (F, Cl, Br, I) normalmente tienen electrones no enlazantes en sus compuestos

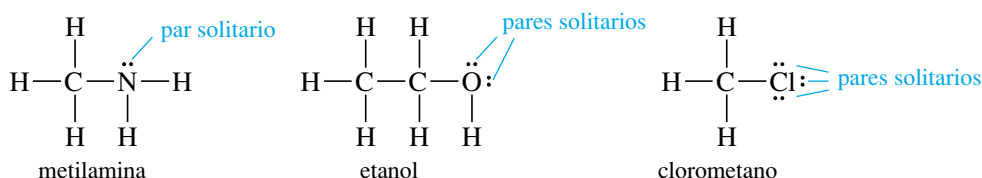
## 1.4 Estructuras de Lewis



## SUGERENCIA PARA RESOLVER PROBLEMAS

Las estructuras de Lewis son la forma de representar los enlaces en química orgánica. Aprender a representarlas de forma rápida y correctamente será muy útil a lo largo de este curso.

estables. Estos pares solitarios de electrones no enlazantes ayudan a determinar la reactividad de sus compuestos. Las estructuras de Lewis siguientes muestran un par solitario de electrones en el átomo de nitrógeno de la metilamina y dos pares solitarios en el átomo de oxígeno del etanol. Los átomos de los halógenos normalmente tienen tres pares solitarios, como se muestra en la estructura del clorometano.



Una estructura de Lewis correcta debería mostrar los pares solitarios de electrones. Los químicos orgánicos a menudo dibujan estructuras de Lewis omitiendo la mayoría o todos los pares solitarios de electrones. Éstas no son estructuras correctas de Lewis porque uno se ha de imaginar el número de electrones no enlazantes.

### PROBLEMA 1.2

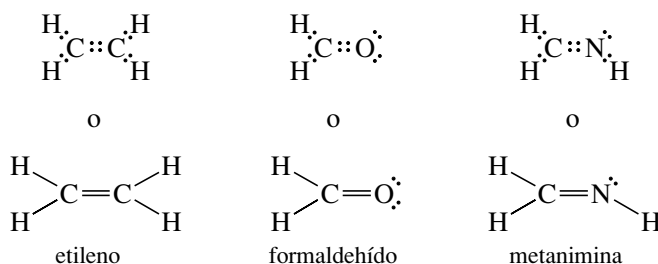
Dibuje las estructuras de Lewis de los siguientes compuestos:

- |  |  |
|--|--|
| (a) amoníaco, $\text{NH}_3$                        | (b) agua, $\text{H}_2\text{O}$                               |
| (c) ión hidronio, $\text{H}_3\text{O}^+$           | (d) propano, $\text{C}_3\text{H}_8$                          |
| (e) etilamina, $\text{CH}_3\text{CH}_2\text{NH}_2$ | (f) dimetil éter, $\text{CH}_3\text{OCH}_3$                  |
| (g) fluoroetano, $\text{CH}_3\text{CH}_2\text{F}$  | (h) 2-propanol, $\text{CH}_3\text{CH}(\text{OH})\text{CH}_3$ |
| (i) borano, $\text{BH}_3$                          | (j) trifluoruro de boro, $\text{BF}_3$                       |

Explique qué es inusual en el enlace de los compuestos (i) y (j).

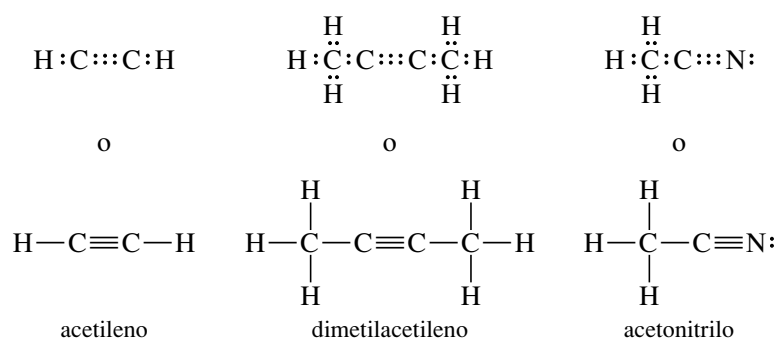
## 1.5 Enlace múltiple

Al representar las estructuras de Lewis en la Sección 1.4, se pusieron un par de electrones entre cada dos átomos. La compartición de un par de electrones entre dos átomos se conoce como **enlace sencillo**. Muchas moléculas comparten con sus átomos adyacentes dos o incluso tres pares de electrones; cuando se comparten dos pares se da el nombre de **enlace doble** y cuando se comparten tres pares se da el nombre de **enlace triple**. El etileno ( $\text{C}_2\text{H}_4$ ) es un compuesto orgánico con un doble enlace. Cuando se representan las estructuras de Lewis para el etileno, la única forma de conseguir que los dos átomos de carbono tengan octetos es mediante la compartición de dos pares de electrones. El ejemplo siguiente muestra compuestos orgánicos con dobles enlaces. En cada caso, se comparten cuatro electrones (dos pares) entre dos átomos para formar octetos. Una doble línea (=) simboliza el doble enlace.



El acetileno, cuando se combina con el oxígeno, arde con una llama intensa que tiene diversas aplicaciones. Se puede utilizar para soldar las piezas de un puente bajo el agua o para reparar las tuberías de un oleoducto en Siberia.

El acetileno ( $\text{C}_2\text{H}_2$ ) tiene un triple enlace. Su estructura de Lewis muestra los tres pares de electrones entre los dos átomos de carbono para que formen un octeto. Una línea triple ( $\equiv$ ) simboliza el triple enlace.



Todas estas estructuras de Lewis muestran que el carbono normalmente forma cuatro enlaces en compuestos orgánicos neutros. El nitrógeno generalmente forma tres enlaces y el oxígeno dos. El hidrógeno y los halógenos normalmente forman un enlace. El número de enlaces que normalmente puede formar un átomo se conoce como **valencia**. El carbono es tetravalente, el nitrógeno trivalente, el oxígeno divalente, y el hidrógeno y los halógenos monovalentes. Si se recuerda el número usual de enlaces de estos elementos, se podrán escribir estructuras orgánicas con mucha facilidad. Si una estructura se representa de forma que cada átomo tenga el número de enlaces que le corresponden, la estructura de Lewis será correcta.

### RESUMEN Modelos de enlace más frecuentes (sin carga)

	$\begin{array}{c}   \\ -\text{C}- \\   \end{array}$	$\begin{array}{c} \cdot\cdot \\ -\text{N}- \\   \end{array}$	$\begin{array}{c} \cdot\cdot \\ -\text{O}- \\ \cdot\cdot \end{array}$	$-\text{H}$	$\begin{array}{c} \cdot\cdot \\ -\text{Cl}: \end{array}$
	carbono	nitrógeno	oxígeno	hidrógeno	halógenos
valencia:	4	3	2	1	1
pares solitarios:	0	1	2	0	3

### SUGERENCIA PARA RESOLVER PROBLEMAS

Estos «números de enlaces usuales» pueden ser sencillos o estar combinados en dobles y triples enlaces. Por ejemplo, los tres enlaces del nitrógeno podrían corresponder a tres enlaces sencillos, a un enlace sencillo y uno doble, o a un triple enlace ( $:\text{N}\equiv\text{N}:$ ). En los problemas hay que considerar todas las posibilidades.

### PROBLEMA 1.3

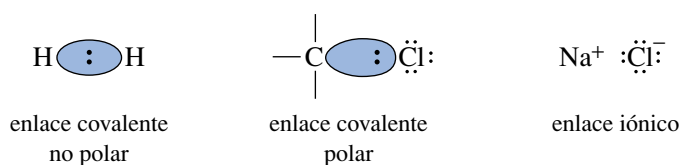
Escriba la estructura de Lewis para cada una de las siguientes fórmulas moleculares:

- |   |   |                            |
|---|---|----------------------------|
| (a) $\text{N}_2$                                | (b) $\text{HCN}$                              | (c) $\text{HONO}$          |
| (d) $\text{CO}_2$                               | (e) $\text{H}_2\text{CNH}$                    | (f) $\text{HCO}_2\text{H}$ |
| (g) $\text{C}_2\text{H}_3\text{Cl}$             | (h) $\text{HNNH}$                             | (i) $\text{C}_3\text{H}_6$ |
| (j) $\text{C}_3\text{H}_4$ (dos dobles enlaces) | (k) $\text{C}_3\text{H}_4$ (un triple enlace) |                            |

### PROBLEMA 1.4

Rodee con un círculo los pares solitarios (pares de electrones no enlazantes) en las estructuras representadas en el Problema 1.3.

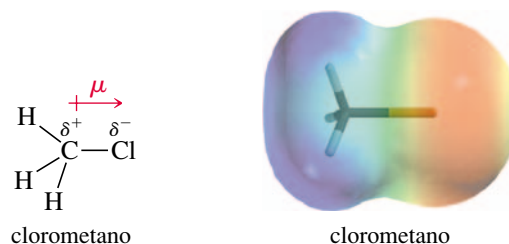
Un enlace cuyos electrones están igualmente compartidos por los dos átomos recibe el nombre de **enlace covalente no polar**. El enlace en la molécula de  $\text{H}_2$  y el enlace  $\text{C}-\text{C}$  en el etano son enlaces covalentes no polares. En la mayoría de enlaces entre dos elementos diferentes los electrones del enlace están atraídos de forma diferente por cada uno de los dos núcleos. Cuando la compartición del par de electrones del enlace no es igual para los dos átomos, a este enlace se le conoce como **enlace covalente polar**.



## 1.6 La electronegatividad y la polaridad de enlace

► **Figura 1.6**

El clorometano contiene un enlace polar carbono-cloro con una carga negativa parcial en el cloro y una carga positiva parcial en el carbono. El mapa de potencial electrostático muestra una región roja (rica en electrones) alrededor de la carga negativa parcial y una región azul (pobre en electrones) alrededor de la carga positiva parcial. El resto de colores indican valores intermedios de potencial electrostático.



Cuando el carbono se enlaza al cloro, por ejemplo, los electrones de enlace son atraídos más fuertemente hacia el átomo de cloro, por lo que el átomo de carbono adquirirá una pequeña carga positiva parcial y el átomo de cloro esa misma cantidad de carga pero de signo negativo. La Figura 1.6 muestra el enlace polar carbono-cloro del clorometano. Nosotros simbolizaremos la polaridad de enlace por una flecha que tenga como origen la carga positiva del enlace polar, y sobre este origen un signo positivo. La polaridad de un enlace se mide por su **momento dipolar** ( $\mu$ ), definido por el producto de la carga (separación de las cargas  $\delta^+$  y  $\delta^-$ ) y la longitud del enlace. El símbolo  $\delta^+$  significa «una pequeña cantidad de carga positiva» y el símbolo  $\delta^-$  «una pequeña cantidad de carga negativa».

La Figura 1.6 también muestra un **mapa de potencial electrostático (MPE)** para el clorometano, que usa colores para representar la distribución de la carga calculada en una molécula. El rojo indica regiones ricas en electrones y el azul regiones pobres en electrones. El naranja, amarillo y verde indican niveles intermedios de potencial electrostático. En el clorometano, la región roja muestra la carga negativa parcial del cloro y la región azul indica la carga positiva parcial de los átomos de carbono y de hidrógeno.

A menudo se usan las **electronegatividades** como guía para predecir si un determinado enlace será polar y la dirección del momento dipolar. La escala de electronegatividad de Pauling, la que comúnmente utilizan los químicos orgánicos, se basa en las propiedades del enlace y es muy útil para predecir la polaridad de los enlaces covalentes. Los elementos con electronegatividades más altas atraen con más fuerza a los electrones de enlace. No obstante, en un enlace entre dos átomos diferentes, el átomo con la electronegatividad más alta es el extremo negativo del dipolo. La Figura 1.7 muestra las electronegatividades de Pauling para algunos de los elementos importantes de los compuestos orgánicos.

Obsérvese que la electronegatividad aumenta de izquierda a derecha a lo largo de la tabla periódica. El nitrógeno, el oxígeno y los halógenos son más electronegativos que el carbono; el sodio, el litio y el magnesio son menos electronegativos. La electronegatividad del hidrógeno es parecida a la del carbono, por lo que el enlace C—H normalmente se considera no polar. La polaridad de los enlaces y de las moléculas se tratará con más detalle en la Sección 2.9.

**PROBLEMA 1.5**

Haga uso de las electronegatividades para predecir los momentos dipolares de los siguientes enlaces:

- (a) C—Cl      (b) C—O      (c) C—N      (d) C—S      (e) C—B  
(f) N—Cl      (g) N—O      (h) N—S      (i) N—B      (j) B—Cl

► **Figura 1.7**

Electronegatividades de algunos de los elementos que se encuentran en los compuestos orgánicos.

H 2.2						
Li 1.0	Be 1.6	B 1.8	C 2.5	N 3.0	O 3.4	F 4.0
Na 0.9	Mg 1.3	Al 1.6	Si 1.9	P 2.2	S 2.6	Cl 3.2
K 0.8						Br 3.0
						I 2.7

En los enlaces polares, las cargas parciales ( $\delta^+$  y  $\delta^-$ ) de los átomos del enlace son *reales*. Las **cargas formales** proporcionan un método de seguimiento de los electrones, pero pueden corresponder o no a cargas reales. En la mayoría de los casos, si la estructura de Lewis muestra que un átomo tiene una carga formal, quiere decir que tiene parte de esa carga. El concepto de carga formal ayuda a determinar qué átomos tienen mayor cantidad de carga en una molécula y ver que hay átomos cargados en moléculas que son neutras globalmente.

Para calcular las cargas formales, hay que contar cuántos electrones contribuyen a la carga de cada átomo y comparar ese número con el número de electrones de valencia que hay en el átomo neutro y aislado (dado por el número de grupo en la tabla periódica). Los electrones que contribuyen a la carga de un átomo son:

1. *Todos* sus electrones no compartidos (no enlazantes).
2. *La mitad* de los electrones (enlazantes) que comparte con otros átomos, o un electrón de cada par de enlace.

La carga formal de un átomo determinado puede ser calculada mediante la fórmula:

$$\text{carga formal (CF)} = [\text{número de grupo}] - [\text{electrones no enlazantes}] - \frac{1}{2} [\text{electrones compartidos}]$$

### PROBLEMA RESUELTO 1.1

Calcule la carga formal (CF) de cada átomo de las estructuras siguientes:

(a) Metano ( $\text{CH}_4$ )

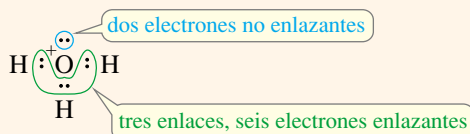


### SOLUCIÓN

Cada átomo de hidrógeno del metano tiene un par enlazante de electrones (dos electrones compartidos). La mitad de los dos electrones compartidos es un electrón de valencia y es lo que el hidrógeno necesita para ser neutro. Los átomos de hidrógeno con un enlace son neutros formalmente:  $\text{CF} = 1 - 0 - 1 = 0$ .

El átomo de carbono tiene cuatro pares de electrones enlazantes (ocho electrones). La mitad de los ocho electrones compartidos, esto es, cuatro electrones son los que el carbono (grupo IVA) necesita para ser neutro. El carbono es formalmente neutro cuando tiene cuatro enlaces:  $\text{CF} = 4 - 0 - \frac{1}{2}(8) = 0$ .

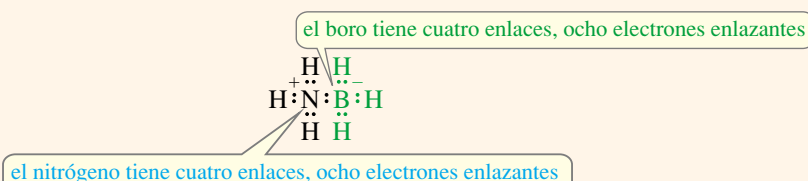
(b) Ión hidronio,  $\text{H}_3\text{O}^+$



### SOLUCIÓN

Cuando se representa la estructura de Lewis para este ión, se utilizan ocho electrones: seis del oxígeno y tres de los hidrógenos, menos uno porque el ión tiene una carga positiva. Cada hidrógeno tiene un enlace y es formalmente neutro. El oxígeno está rodeado por un octeto, con seis electrones enlazantes y dos electrones no enlazantes. La mitad de los electrones enlazantes más todos los electrones no enlazantes contribuyen a la carga:  $6/2 + 2 = 5$ ; pero el oxígeno (grupo VIA) necesita seis electrones de valencia para ser neutro, por este motivo, el átomo de oxígeno tiene una carga formal de  $+1$ :  $\text{CF} = 6 - 2 - \frac{1}{2}(6) = +1$ .

(c)  $\text{H}_3\text{N} - \text{BH}_3$



## 1.7 Cargas formales

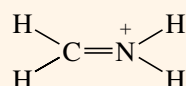
**SOLUCIÓN**

Éste es un compuesto neutro donde los átomos individuales están cargados formalmente. La estructura de Lewis muestra que tanto el nitrógeno como el boro tienen cuatro pares de electrones enlazantes. Los dos átomos, boro y nitrógeno, tienen  $8/2 = 4$  electrones que contribuyen a sus cargas. El nitrógeno (grupo V) necesita cinco electrones de valencia para ser neutro, por lo que su carga formal es  $+1$ . El boro (grupo III) sólo necesita tres electrones de valencia para ser neutro, por lo que su carga formal es  $-1$ .

$$\text{Nitrógeno: } CF = 5 - 0 - \frac{1}{2}(8) = +1$$

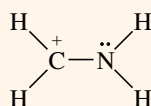
$$\text{Boro: } CF = 3 - 0 - \frac{1}{2}(8) = -1$$

(d)  $[\text{H}_2\text{CNH}_2]^+$

**SOLUCIÓN**

En esta estructura, tanto el carbono como el nitrógeno tienen cuatro pares de electrones enlazantes. Con cuatro enlaces, el carbono es formalmente neutro; no obstante, el nitrógeno es del grupo V, por lo que su carga positiva formal es:  $CF = 5 - 0 - 4 = +1$ .

Este compuesto también podría ser representado con la siguiente estructura de Lewis:



En esta estructura, el átomo de carbono tiene tres enlaces con seis electrones enlazantes que, si se dividen entre dos,  $6/2 = 3$ , se observa que el carbono tiene un electrón menos de los cuatro que necesita para ser neutro formalmente:  $CF = 4 - 0 - \frac{1}{2}(6) = +1$ .

El nitrógeno tiene seis electrones enlazantes y dos electrones no enlazantes. Si se hace el cálculo  $6/2 + 2 = 5$ , se observa que el nitrógeno es neutro en esta segunda estructura:

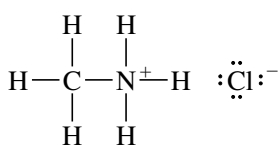
$$CF = 5 - 2 - \frac{1}{2}(6) = 0$$

El significado de estas dos estructuras de Lewis se discute en la Sección 1.9.

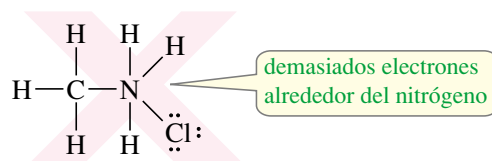
La mayoría de los compuestos orgánicos sólo contienen un número pequeño de elementos bastante comunes, normalmente con el octeto de electrones completo. La tabla resumen de la página siguiente indica la naturaleza de los enlaces más habituales, utilizando líneas para representar los pares de electrones enlazantes. Utilice estas reglas de cálculo de las cargas formales para comprobar las cargas que se dan en las estructuras. Si las estructuras se entienden bien, será fácil representar los compuestos orgánicos y sus iones de forma rápida y correcta.

## 1.8 Estructuras iónicas

Algunos compuestos orgánicos contienen enlaces iónicos. Por ejemplo, la estructura del cloruro de metilamonio ( $\text{CH}_3\text{NH}_3\text{Cl}$ ) no se puede representar si solamente se utilizan enlaces covalentes; esto requeriría que el nitrógeno tuviese cinco enlaces, lo que implicaría diez electrones en la capa de valencia. La estructura correcta contiene un ión cloruro enlazado iónicamente al resto de la estructura.



cloruro de metilamonio



no se puede representar mediante enlaces covalentes

## RESUMEN

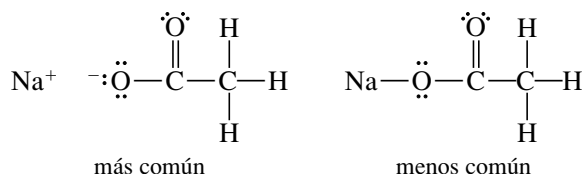
## Modelos de enlace más frecuentes en los compuestos e iones orgánicos

Átomo	Electrones de valencia	Cargado positivamente	Neutro	Cargado negativamente
B	3		(no octeto) $\begin{array}{c} \text{—B—} \\   \end{array}$	$\begin{array}{c}   \\ \text{—B—} \\   \end{array}$
C	4	$\begin{array}{c} + \\ \text{—C—} \\   \end{array}$ (no octeto)	$\begin{array}{c}   \\ \text{—C—} \\   \end{array}$	$\begin{array}{c} \cdot\cdot \\ \text{—C—} \\   \end{array}$
N	5	$\begin{array}{c}   \\ \text{—N}^+ \\   \end{array}$	$\begin{array}{c} \cdot\cdot \\ \text{—N—} \\   \end{array}$	$\begin{array}{c} \cdot\cdot \\ \text{—N—} \\   \end{array}$
O	6	$\begin{array}{c} \cdot\cdot \\ \text{—O}^+ \\   \end{array}$	$\begin{array}{c} \cdot\cdot \\ \text{—O—} \\   \end{array}$	$\begin{array}{c} \cdot\cdot \\ \text{—O—} \\   \end{array}$
halógeno	7	$\begin{array}{c} \cdot\cdot \\ \text{—Cl}^+ \\   \end{array}$	$\begin{array}{c} \cdot\cdot \\ \text{—Cl:} \end{array}$	$\begin{array}{c} \cdot\cdot \\ \text{:Cl:}^- \end{array}$

SUGERENCIA  
PARA RESOLVER PROBLEMAS

Esta tabla es muy importante. Haz un número de problemas suficientes como para familiarizarte con estos modelos de enlace, tal que puedas saber cuándo otros modelos son incorrectos o bien inusuales.

Algunas moléculas se pueden representar tanto en forma covalente como iónica. Por ejemplo, el acetato de sodio ( $\text{NaOCOCH}_3$ ) se puede representar tanto con un enlace covalente como con un enlace iónico entre el sodio y el oxígeno. Como el sodio normalmente forma enlaces iónicos con el oxígeno ( $\text{NaOH}$ ), la estructura con enlace iónico es la que se prefiere. En general, los enlaces entre átomos con gran diferencia de electronegatividad (2 o más) normalmente se representan como compuestos iónicos.



## PROBLEMA 1.6

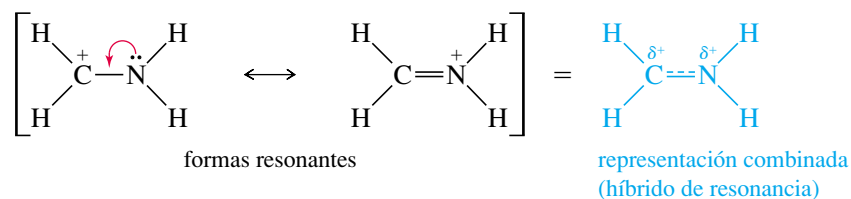
Dibuje las estructuras de Lewis de los siguientes compuestos e iones, diciendo cuál es su carga formal apropiada:

- |   |                                 |
|---|---------------------------------|
| (a) $[\text{CH}_3\text{OH}_2]^+$          | (b) $\text{NH}_4\text{Cl}$      |
| (c) $(\text{CH}_3)_2\text{NH}_2\text{Cl}$ | (d) $\text{NaOCH}_3$            |
| (e) $^+\text{CH}_3$                       | (f) $^-\text{CH}_3$             |
| (g) $\text{NaBH}_4$                       | (h) $\text{NaBH}_3\text{CN}$    |
| (i) $(\text{CH}_3)_2\text{O—BF}_3$        | (j) $[\text{HONH}_3]^+$         |
| (k) $\text{KOC}(\text{CH}_3)_3$           | (l) $[\text{H}_2\text{C=OH}]^+$ |

## 1.9A Híbridos de resonancia

Algunas de las estructuras de los compuestos no es adecuado representarlas mediante una sola estructura de Lewis. Cuando son posibles dos o más estructuras de enlace de valencia, que difieren sólo en la colocación de los electrones, la molécula suele mostrar características de las dos estructuras. A estas estructuras diferentes se las conoce como **estructuras de resonancia** o **formas resonantes**, ya que no son compuestos diferentes, sino formas diferentes de representar el mismo compuesto. La molécula real se dice que corresponde a un **híbrido de resonancia** de sus formas resonantes. En el Problema resuelto 1.1(d) se mostró cómo el ión  $[\text{H}_2\text{CNH}_2]^+$  se podía representar por cualquiera de las siguientes formas de resonancia:

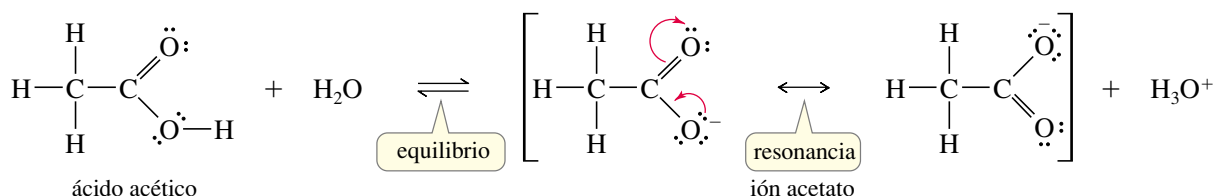
1.9  
Resonancia



La estructura real de este ión es un híbrido de resonancia de las dos estructuras. En la molécula real, la carga positiva está **deslocalizada** (extendida) entre el átomo de carbono y el de nitrógeno. En la forma resonante de la izquierda, la carga positiva está en el carbono, pero el carbono no tiene un octeto. Los electrones no enlazantes del nitrógeno se pueden mover por el enlace (tal como indica la flecha roja) dando una segunda estructura con un doble enlace entre el nitrógeno que tiene carga positiva y el carbono que posee un octeto. La representación combinada de las dos formas de resonancia en una sola representación da lugar a una carga compartida entre el nitrógeno y el carbono.

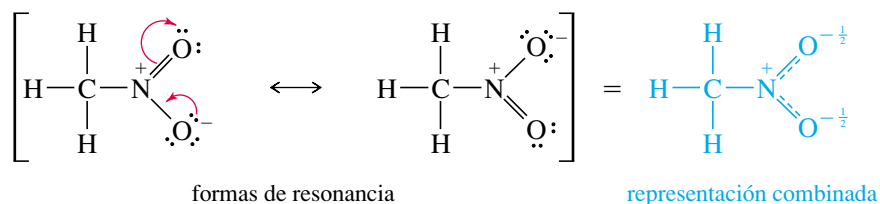
El extender la carga positiva sobre dos átomos hace que el ión sea más estable que en el caso de que la carga positiva estuviera localizada solamente sobre el carbono o sobre el nitrógeno. Se dice que este catión está **estabilizado por resonancia**. La resonancia es más importante cuando permite que una carga esté deslocalizada entre dos o más átomos, como en el ejemplo mencionado.

La estabilización por resonancia desempeña un papel crucial en la química orgánica, especialmente en la química de compuestos que tienen dobles enlaces. Se usará frecuentemente el concepto de resonancia a lo largo de este curso. Por ejemplo, la acidez del ácido acético (véase abajo) se incrementa por efecto de la resonancia. Cuando el ácido acético pierde un protón, el ión acetato resultante tiene una carga negativa deslocalizada sobre los dos átomos de oxígeno. Cada átomo de oxígeno posee la mitad de la carga negativa y su deslocalización estabiliza el ión. Cada uno de los enlaces carbono-oxígeno es intermedio entre un enlace doble y un enlace sencillo, por lo que se dice que su *orden de enlace* es de  $1\frac{1}{2}$ .



Se usará una sola flecha con doble punta entre las formas de resonancia (a menudo puestas entre corchetes) para indicar que la estructura real es un híbrido de las estructuras de Lewis representadas. Por otra parte, un equilibrio se representará por dos flechas con sentidos opuestos.

Algunas moléculas sin carga también tienen estructuras de resonancia estabilizadas con la misma carga formal positiva y negativa. Se pueden representar dos estructuras de Lewis para el nitrometano ( $\text{CH}_3\text{NO}_2$ ), pero las dos estructuras tienen una carga positiva formal en el nitrógeno y una carga negativa en uno de los oxígenos. Por tanto, el nitrometano tiene una carga positiva en el átomo de nitrógeno y una carga negativa extendida por igual sobre los dos átomos de oxígeno. Los enlaces N—O están entre un enlace sencillo y uno doble, tal como se indica en la representación combinada siguiente:



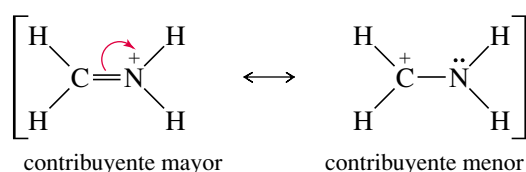
Recuerde que las formas de resonancia individuales no existen como especies químicas independientes. La molécula no «resuena» entre esas estructuras, es un híbrido con



características de ambas estructuras. Una analogía sería una mula, que es un híbrido de un caballo y un burro. La mula no «resuena» entre parecerse a un caballo o a un burro; simplemente es una mula, con el amplio dorso de un caballo y las grandes orejas de un burro.

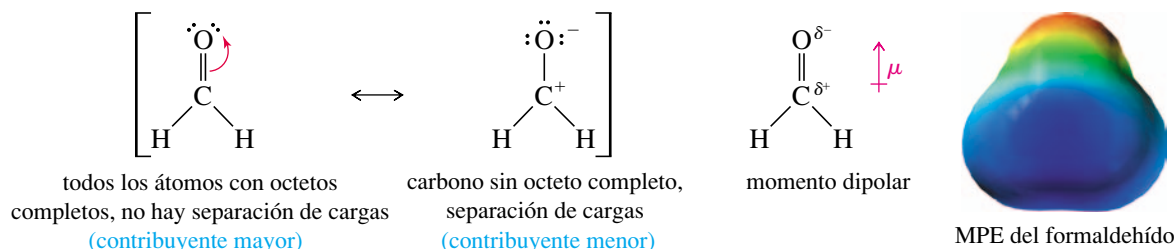
### 1.9B Contribución mayor o menor de las formas resonantes al híbrido de resonancia

Dos o más estructuras de Lewis correctas para un mismo compuesto pueden o no representar distribuciones de electrones de igual energía. A pesar de que formas de resonancia separadas no existen, se pueden estimar sus energías relativas como si existieran. La mayoría de las formas de resonancia estables son representaciones más cercanas de la molécula real que las menos estables. Las dos formas de resonancia del apartado anterior, para el ión acetato, tienen enlaces similares e idéntica energía. Lo mismo se puede decir para las dos formas de resonancia del nitrometano. Las formas de resonancia siguientes, por el contrario, tienen enlaces diferentes.



Las estructuras anteriores no tienen la misma energía estimada. La primera estructura tiene la carga positiva en el nitrógeno. La segunda tiene la carga positiva en el carbono, y el átomo de carbono no posee un octeto completo. La primera estructura es más estable ya que tiene un enlace adicional y todos los átomos tienen octetos completos. Muchos iones estables tienen una carga positiva en el átomo de nitrógeno con cuatro enlaces (*véase* la tabla resumen de la página 13). A la forma de resonancia más estable se la conoce como la **contribuyente mayor** y a la forma menos estable como la **contribuyente menor**. La estructura del compuesto real se parece más al contribuyente mayor que al contribuyente menor.

Muchas moléculas orgánicas tienen contribuyentes de resonancia mayor y menor. El formaldehído ( $\text{H}_2\text{C}=\text{O}$ ) se puede representar con una carga negativa en el oxígeno, equilibrada por una carga positiva en el carbono. Esta forma de resonancia polar tiene mayor energía estimada que la estructura con doble enlace, porque tiene separación de cargas, menos enlaces y un átomo de carbono cargado positivamente con un octeto incompleto. La estructura con cargas separadas es solamente un contribuyente menor, pero ayuda a explicar por qué el enlace  $\text{C}=\text{O}$  del formaldehído es muy polar, con una carga positiva parcial en el carbono y una carga negativa parcial en el oxígeno. El mapa de potencial electrostático (MPE) también muestra una región rica en electrones (rojo) alrededor del oxígeno y una región pobre en electrones (azul) alrededor del carbono en el formaldehído.



Cuando se representan las formas de resonancia, se intenta dibujar estructuras que sean lo más bajas posible en energía. Las mejores candidatas son las que tienen un número máximo de octetos y el máximo número de enlaces. Además, las estructuras tienen que tener la mínima cantidad de separación de cargas.

*Sólo los electrones pueden estar deslocalizados.* Al contrario que los electrones, los núcleos no pueden estar deslocalizados, deben permanecer en el mismo lugar, con las mismas distancias de enlace y los mismos ángulos en todos los contribuyentes a la resonancia. Las reglas generales siguientes serán útiles para representar estructuras de resonancias.



## SUGERENCIA PARA RESOLVER PROBLEMAS

Para comparar las formas de resonancia se pueden utilizar los siguientes criterios, comenzando por el más importante:

1. Tantos octetos como sea posible.
2. Tantos enlaces como sea posible.
3. Si hay carga negativa se coloca en los átomos electronegativos.
4. La menor separación de cargas posible.

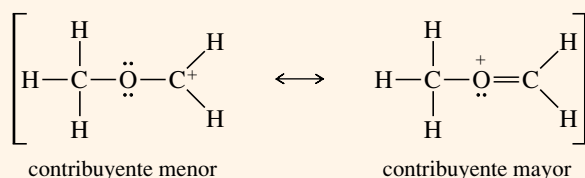
1. Todas las estructuras de resonancia deben ser estructuras de Lewis válidas para el compuesto.
2. Sólo se puede cambiar la posición de los electrones de una estructura a otra (los electrones de los dobles enlaces y pares solitarios son los que se cambian con más frecuencia). El núcleo no se puede cambiar de posición y los ángulos de enlace han de ser los mismos.
3. El número de electrones desapareados (si hay alguno) debe permanecer igual. La mayoría de los compuestos estables no tienen electrones desapareados y todos los electrones deben permanecer apareados en todas las estructuras de resonancia.
4. El contribuyente mayor a la resonancia es el que tiene menor energía.  
Los buenos contribuyentes generalmente tienen todos los octetos satisfechos, con el máximo número de enlaces covalentes que sea posible y con una separación de cargas lo menor posible. Las cargas negativas son más estables en los átomos más electronegativos.
5. La estabilización por resonancia es más importante cuando sirve para deslocalizar una carga entre dos o más átomos.

### PROBLEMA RESUELTO 1.2

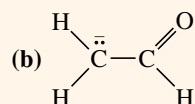
Para cada uno de los siguientes compuestos, represente las formas de resonancia importantes. Indique qué estructuras tienen contribuyentes mayores y menores, o si tienen la misma energía.

(a)  $[\text{CH}_3\text{OCH}_2]^+$

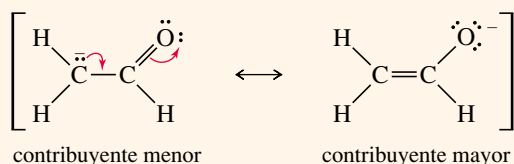
#### SOLUCIÓN



La primera estructura (menor) tiene un átomo de carbono con sólo seis electrones a su alrededor. La segunda estructura (mayor) tiene octetos en todos los átomos y un enlace adicional.



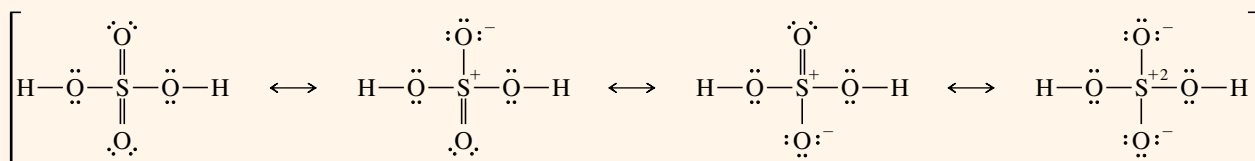
#### SOLUCIÓN



Las dos estructuras tienen octetos en el átomo de oxígeno y en el de carbono, y tienen el mismo número de enlaces. La primera estructura tiene la carga negativa en el carbono y la segunda la tiene en el oxígeno. El oxígeno es más electronegativo que el carbono, por lo tanto, la segunda estructura es el contribuyente mayor.

(c)  $\text{H}_2\text{SO}_4$

#### SOLUCIÓN



La primera estructura, con más enlaces y menor separación de carga, es posible porque el azufre es un elemento de la tercera fila de la tabla periódica con orbitales *d* accesibles, lo que le da la posibilidad de expandir aparentemente su octeto. Por ejemplo, el  $\text{SF}_6$  es un compuesto estable con 12 electrones alrededor del azufre. Sin embargo, algunos cálculos teóricos sugieren que la última estructura representada, con octetos en todos los átomos, podría ser la contribuyente mayor a la resonancia. No se puede predecir siempre el contribuyente mayor de un híbrido de resonancia.

**PROBLEMA 1.7**

Represente las formas de resonancia importantes de las siguientes moléculas e iones:

- (a)  $\text{CO}_3^{2-}$  (b)  $\text{NO}_3^-$  (c)  $\text{NO}_2^-$  (d)  $\text{H}_2\text{C}=\text{CH}-\text{CH}_2^+$   
 (e)  $\text{H}_2\text{C}=\text{CH}-\text{CH}_2^-$  (f)  $\text{SO}_4^{2-}$  (g)  $[\text{CH}_3\text{C}(\text{OCH}_3)_2]^+$

**PROBLEMA 1.8**

Para cada uno de los siguientes compuestos, represente las formas de resonancia importantes. Indique qué estructuras son las contribuyentes mayores y menores a la resonancia, o si tienen la misma energía.

- (a)  $[\text{H}_2\text{CNO}_2]^-$  (b)  $\text{H}_2\text{C}=\text{CH}-\text{NO}_2$  (c)  $[\text{H}_2\text{COH}]^+$   
 (d)  $\text{H}_2\text{CNN}$  (e)  $[\text{H}_2\text{CCN}]^-$  (f)  $\text{H}_2\text{N}-\overset{+}{\text{CH}}-\text{CH}=\text{CH}-\text{NH}_2$   
 (g)  $\text{H}-\overset{\text{O}}{\parallel}{\text{C}}-\overset{-}{\text{CH}}-\overset{\text{O}}{\parallel}{\text{C}}-\text{H}$  (h)  $\text{H}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$

**SUGERENCIA****PARA RESOLVER PROBLEMAS**

Quando se representan formas de resonancia para iones, observe cómo se puede deslocalizar la carga entre varios átomos. Intente colocar una carga negativa sobre elementos electronegativos como el oxígeno y el nitrógeno. Intente, así mismo, colocar una carga positiva sobre todos los carbonos que sea posible, pero especialmente sobre los átomos que puedan alojar la carga positiva y tener un octeto completo; por ejemplo, el oxígeno (con tres enlaces) o el nitrógeno (con cuatro enlaces).

Los químicos orgánicos utilizan varias clases de fórmulas para representar los compuestos orgánicos. Algunas de estas fórmulas incluyen una notación específica que requiere una explicación. Las **fórmulas estructurales** indican qué átomos están enlazados a otros. Hay dos tipos de fórmulas estructurales: las estructuras de Lewis completas y las fórmulas estructurales condensadas. Además, hay varias formas de representar fórmulas estructurales condensadas. Según se ha visto, una estructura de Lewis simboliza un par de electrones enlazantes como un par de puntos o como una línea (—). Los pares solitarios de electrones se muestran como pares de puntos.

**1.10****Fórmulas estructurales****1.10A Fórmulas estructurales condensadas**

Las **fórmulas estructurales condensadas** (Tabla 1.2) se representan sin mostrar todos los enlaces individuales. En una estructura condensada, cada átomo central se representa junto a los átomos a los que está enlazado. Los átomos enlazados a un átomo central a menudo se escriben a continuación del átomo central ( $\text{CH}_3\text{CH}_3$  en lugar de  $\text{H}_3\text{C}-\text{CH}_3$ ) incluso aunque no sea el orden del verdadero enlace. En muchos casos, si hay dos o más grupos idénticos, se puede utilizar un paréntesis y un subíndice para representar a todos estos grupos. Los electrones no enlazantes raramente se representan en las fórmulas estructurales condensadas.

**TABLA 1.2** Ejemplos de fórmulas estructurales condensadas

Compuesto	Estructura de Lewis	Fórmula estructural condensada
etano	$\begin{array}{c} \text{H} \quad \text{H} \\   \quad   \\ \text{H}-\text{C}-\text{C}-\text{H} \\   \quad   \\ \text{H} \quad \text{H} \end{array}$	$\text{CH}_3\text{CH}_3$
isobutano	$\begin{array}{c} \text{H} \quad \text{H} \quad \text{H} \\   \quad   \quad   \\ \text{H}-\text{C}-\text{C}-\text{C}-\text{H} \\   \quad   \quad   \\ \text{H} \quad \text{H} \quad \text{H} \\   \\ \text{H}-\text{C}-\text{H} \\   \\ \text{H} \end{array}$	$(\text{CH}_3)_3\text{CH}$
n-hexano	$\begin{array}{c} \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \\   \quad   \quad   \quad   \quad   \quad   \\ \text{H}-\text{C}-\text{C}-\text{C}-\text{C}-\text{C}-\text{C}-\text{H} \\   \quad   \quad   \quad   \quad   \quad   \\ \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \end{array}$	$\text{CH}_3(\text{CH}_2)_4\text{CH}_3$

(continúa en la página siguiente)

**TABLA 1.2** (continuación)

Compuesto	Estructura de Lewis	Fórmula estructural condensada
dietil éter	$  \begin{array}{ccccccc}  & \text{H} & \text{H} & & \text{H} & \text{H} & \\  &   &   & &   &   & \\  \text{H} & - \text{C} & - \text{C} & - \ddot{\text{O}} & - \text{C} & - \text{C} & - \text{H} \\  &   &   & &   &   & \\  & \text{H} & \text{H} & & \text{H} & \text{H} &   \end{array}  $	$\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$ o $\text{CH}_3\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_3$ o $(\text{CH}_3\text{CH}_2)_2\text{O}$
etanol	$  \begin{array}{ccccccc}  & \text{H} & \text{H} & & & & \\  &   &   & & & & \\  \text{H} & - \text{C} & - \text{C} & - \ddot{\text{O}} & - \text{H} \\  &   &   & & & & \\  & \text{H} & \text{H} & & & &   \end{array}  $	$\text{CH}_3\text{CH}_2\text{OH}$
alcohol isopropílico	$  \begin{array}{ccccccc}  & \text{H} & & \ddot{\text{O}} & - \text{H} & \text{H} & \\  &   & &   & &   & \\  \text{H} & - \text{C} & - \text{C} & - & \text{C} & - \text{H} \\  &   &   & &   & \\  & \text{H} & \text{H} & & \text{H} &   \end{array}  $	$(\text{CH}_3)_2\text{CHOH}$
dimetilamina	$  \begin{array}{ccccccc}  & \text{H} & & & \text{H} & & \\  &   & & &   & & \\  \text{H} & - \text{C} & - \ddot{\text{N}} & - & \text{C} & - \text{H} \\  &   & & &   & \\  & \text{H} & & & \text{H} &   \end{array}  $	$(\text{CH}_3)_2\text{NH}$

Cuando se escribe una fórmula estructural condensada para un compuesto que contiene enlaces dobles o triples, los enlaces múltiples con frecuencia se representan igual que en las estructuras de Lewis. La Tabla 1.3 muestra ejemplos de fórmulas estructurales condensadas que contienen enlaces múltiples. Observe que el grupo  $-\text{CHO}$  de un aldehído y el grupo  $-\text{COOH}$  de un ácido carboxílico se enlazan de forma diferente a como sugiere la notación condensada.

Como se puede observar en las Tablas 1.2 y 1.3, la diferencia entre una fórmula estructural de Lewis completa y una fórmula estructural condensada puede ser confusa. Los químicos con frecuencia representan las fórmulas con algunas partes condensadas y otras

**TABLA 1.3** Fórmulas estructurales condensadas para dobles y triples enlaces

Compuesto	Estructura de Lewis	Fórmula estructural condensada
2-buteno	$  \begin{array}{ccccccc}  & \text{H} & \text{H} & & \text{H} & & \\  &   &   & &   & & \\  \text{H} & - \text{C} & - \text{C} & = \text{C} & - \text{C} & - \text{H} \\  &   & &   &   & \\  & \text{H} & & \text{H} & \text{H} &   \end{array}  $	$\text{CH}_3\text{CHCHCH}_3$ o $\text{CH}_3\text{CH}=\text{CHCH}_3$
acetonitrilo	$  \begin{array}{ccccccc}  & \text{H} & & & & & \\  &   & & & & & \\  \text{H} & - \text{C} & - \text{C} & \equiv \text{N} & : \\  &   & & & & & \\  & \text{H} & & & & &   \end{array}  $	$\text{CH}_3\text{CN}$ o $\text{CH}_3\text{C}\equiv\text{N}$
acetaldehído	$  \begin{array}{ccccccc}  & \text{H} & & \ddot{\text{O}} & & & \\  &   & &    & & & \\  \text{H} & - \text{C} & - & \text{C} & - \text{H} \\  &   & & & & & \\  & \text{H} & & & & &   \end{array}  $	$\text{CH}_3\text{CHO}$ o $\text{CH}_3\overset{\text{O}}{\underset{  }{\text{C}}}\text{H}$
acetona	$  \begin{array}{ccccccc}  & \text{H} & & \ddot{\text{O}} & & \text{H} & \\  &   & &    & &   & \\  \text{H} & - \text{C} & - & \text{C} & - & \text{C} & - \text{H} \\  &   & & & &   & \\  & \text{H} & & & & \text{H} &   \end{array}  $	$\text{CH}_3\text{COCH}_3$ o $\text{CH}_3\overset{\text{O}}{\underset{  }{\text{C}}}\text{CH}_3$
ácido acético	$  \begin{array}{ccccccc}  & \text{H} & & \ddot{\text{O}} & & & \\  &   & &    & & & \\  \text{H} & - \text{C} & - & \text{C} & - \ddot{\text{O}} & - \text{H} \\  &   & & & & & \\  & \text{H} & & & & &   \end{array}  $	$\text{CH}_3\text{COOH}$ o $\text{CH}_3\overset{\text{O}}{\underset{  }{\text{C}}}-\text{OH}$ o $\text{CH}_3\text{CO}_2\text{H}$

completamente desarrolladas. El estudiante debería trabajar con las diferentes formas de representar las fórmulas para entender su significado.

### PROBLEMA 1.9

Represente las estructuras de Lewis completas para las siguientes fórmulas estructurales condensadas:

- (a)  $\text{CH}_3(\text{CH}_2)_3\text{CH}(\text{CH}_3)_2$  (b)  $(\text{CH}_3)_2\text{CHCH}_2\text{Cl}$  (c)  $\text{CH}_3\text{CH}_2\text{COCHCH}_2$   
 (d)  $\text{CH}_3\text{CH}_2\text{CHO}$  (e)  $\text{CH}_3\text{COCN}$  (f)  $(\text{CH}_3)_3\text{CCOOH}$  (g)  $(\text{CH}_3\text{CH}_2)_2\text{CO}$

### 1.10B Fórmulas lineoangulares

Otra forma de representar las estructuras orgánicas es la **fórmula lineoangular**, algunas veces llamada **estructura esquelética** o de barras. Las fórmulas lineoangulares con frecuencia se usan en los compuestos cíclicos y muy ocasionalmente en los lineales. En una fórmula lineoangular, los enlaces están representados por líneas y los átomos de carbono vienen dados por los vértices o puntos de encuentro de dos líneas, o el punto del principio o final de la línea en el caso de los extremos. Los átomos de nitrógeno, de oxígeno y los halógenos se escriben con su símbolo, pero los átomos de hidrógeno frecuentemente no se simbolizan a no ser que vayan unidos a elementos que se han simbolizado. Se supone que cada átomo de carbono tiene los suficientes átomos de hidrógeno para que el total de sus enlaces sea cuatro. Los electrones no enlazantes raramente se representan. La Tabla 1.4 muestra algunos ejemplos de estas representaciones lineoangulares.

**TABLA 1.4** Ejemplos de representaciones lineoangulares

Compuesto	Estructura condensada	Fórmula lineoangular
hexano	$\text{CH}_3(\text{CH}_2)_4\text{CH}_3$	
2-hexeno	$\text{CH}_3\text{CH}=\text{CHCH}_2\text{CH}_2\text{CH}_3$	
3-hexanol	$\text{CH}_3\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{CH}_2\text{CH}_3$	
2-ciclohexenona		
2-metilciclohexanol		
ácido nicotínico (vitamina, también llamada niacina)		

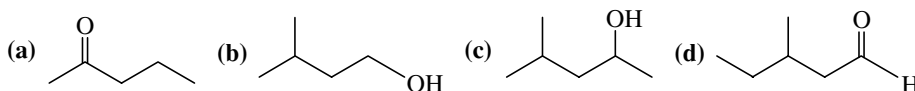
### PROBLEMA 1.10

Escriba la estructura de Lewis correspondiente a las siguientes estructuras lineoangulares:

- (a)
- (b)
- (c)
- (d)
- (e)
- (f)
- (g)
- (h)

**PROBLEMA 1.11**

Represente las fórmulas estructurales condensadas correspondientes a las siguientes estructuras lineoangulares:



## 1.11

### Fórmulas moleculares y fórmulas empíricas

Antes de poder escribir las posibles fórmulas estructurales de un compuesto, se necesita saber su fórmula molecular. La **fórmula molecular** simplemente informa del número de átomos de cada elemento que hay en una molécula de un compuesto. Por ejemplo, la fórmula molecular del 1-butanol es  $C_4H_{10}O$ .



1-butanol, fórmula molecular  $C_4H_{10}O$

**Cálculo de la fórmula empírica** Las fórmulas moleculares se pueden determinar mediante un proceso que consta de dos pasos. El primer paso es la determinación de la **fórmula empírica**, o relación relativa entre los elementos presentes en la molécula. Suponga, por ejemplo, que en un compuesto desconocido, por análisis elemental cuantitativo, se encontró que contenía un 40.00% de carbono y un 6.67% de hidrógeno. La masa restante, 53.33%, se supone que era oxígeno. Para pasar esos números a una fórmula empírica, se puede seguir un procedimiento simple:

1. Suponga que la muestra contiene 100 g, por lo que los valores porcentuales dan el número de gramos de cada elemento. Dividiendo el número de gramos de cada elemento por la masa atómica se obtiene el número de moles de ese átomo en los 100 g de muestra.
2. Divida cada uno de los números de moles obtenidos en el paso anterior por el número más pequeño y redondee a la cifra entera más próxima. Este paso ha de conducir a la relación existente, expresada en números enteros, entre los elementos de la molécula.

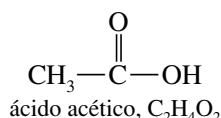
Para el compuesto desconocido, con los datos anteriores y siguiendo los pasos indicados, se obtendrían los siguientes resultados:

$$\begin{aligned} \frac{40.0 \text{ g C}}{12.0 \text{ g/mol}} &= 3.33 \text{ mol C}; & \frac{3.33 \text{ mol}}{3.33 \text{ mol}} &= 1 \\ \frac{6.67 \text{ g H}}{1.01 \text{ g/mol}} &= 6.60 \text{ mol H}; & \frac{6.60 \text{ mol}}{3.33 \text{ mol}} &= 1.98 \approx 2 \\ \frac{53.3 \text{ g O}}{16.0 \text{ g/mol}} &= 3.33 \text{ mol O}; & \frac{3.33 \text{ mol}}{3.33 \text{ mol}} &= 1 \end{aligned}$$

En el primer cálculo se divide el número de gramos de carbono por 12, el número de gramos de hidrógeno por 1 y el número de gramos de oxígeno por 16. Se comparan los resultados dividiendo todos los valores obtenidos por el número más pequeño, 3.33. El resultado final da una relación de un átomo de carbono por dos de hidrógeno y uno de oxígeno. Este resultado nos dice que la fórmula empírica es  $C_1H_2O_1$  o  $CH_2O$ , que muestra solamente la relación de los elementos. La fórmula molecular puede ser un múltiplo cualquiera de la fórmula empírica, porque cualquier múltiplo también tiene la misma relación numérica entre los átomos de sus elementos. Fórmulas moleculares posibles son  $CH_2O$ ,  $C_2H_4O_2$ ,  $C_3H_6O_3$ ,  $C_4H_8O_4$ , etc.

**Cálculo de la fórmula molecular** ¿Cómo se sabe cuál es la fórmula molecular correcta? Se puede elegir el verdadero múltiplo de la fórmula empírica cuando se conoce la masa molecular. Las masas moleculares de una sustancia se pueden determinar por métodos como el *descenso crioscópico* o el *aumento ebulloscópico* de un disolvente cuando contiene la sustancia desconocida a una concentración molar. Si el compuesto es volátil, se puede convertir en gas y utilizar su volumen para determinar el número de moles por la *ley de los gases ideales*. En la actualidad existen métodos entre los que se incluye la *espectrometría de masas*, que será tratada en el Capítulo 11.

Para el ejemplo anterior (fórmula empírica:  $\text{CH}_2\text{O}$ ) supondremos que la masa molecular es aproximadamente 60. La masa de una unidad de  $\text{CH}_2\text{O}$  es 30, por lo que el compuesto contendrá el doble número de átomos. La fórmula molecular será  $\text{C}_2\text{H}_4\text{O}_2$ . Este compuesto podría ser el ácido acético.



En los Capítulos 12, 13 y 15 se usarán técnicas espectroscópicas para determinar la estructura completa de un compuesto una vez que se conozca su fórmula molecular.

### PROBLEMA 1.12

Escriba la fórmula empírica y la fórmula molecular a partir de los análisis elementales siguientes. En cada caso, proponga al menos una estructura que corresponda a la fórmula molecular.

	C	H	N	Cl	PM(*)
(a)	40.0%	6.67%	0	0	90
(b)	32.0%	6.67%	18.7%	0	75
(c)	37.2%	7.75%	0	55.0%	64
(d)	38.4%	4.80%	0	56.8%	125

(\*) Peso molecular.

### SUGERENCIA

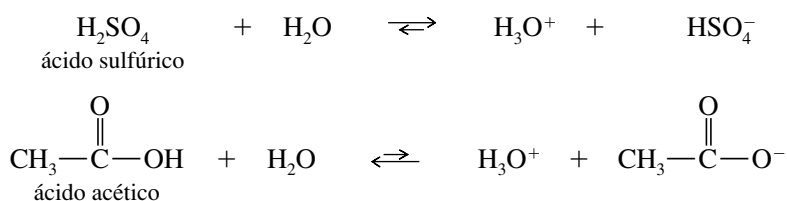
#### PARA RESOLVER PROBLEMAS

Si un análisis elemental no suma el 100%, el porcentaje que falta se supone que es de oxígeno.

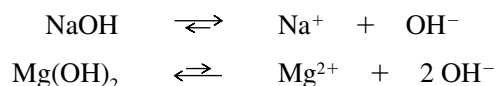
Las propiedades y la reactividad de los ácidos y de las bases son fundamentales para el estudio de la química orgánica. Hay que saber exactamente qué quieren decir los términos **ácido** y **base**. La mayoría de la gente estaría de acuerdo en que el  $\text{H}_2\text{SO}_4$  es un ácido y el  $\text{NaOH}$  una base. ¿El  $\text{BF}_3$  es un ácido o es una base? ¿El etileno ( $\text{H}_2\text{C}=\text{CH}_2$ ) es un ácido o una base? Para responder a estas preguntas se necesitan entender las tres definiciones diferentes de los ácidos y de las bases: la definición de Arrhenius, la de Brønsted-Lowry y la de Lewis.

La primera clasificación de los compuestos ácidos se hizo basándose en su sabor agrio. Los términos latinos *acidus* (agrio) y *acetum* (vinagre) dieron lugar a los términos actuales de *ácido* y *ácido acético*. Los compuestos alcalinos (bases) eran sustancias que neutralizaban a los ácidos, tales como la caliza y las cenizas de las plantas (en árabe, *al kalai*).

La *teoría de Arrhenius* se desarrolló al final del siglo diecinueve y definía los ácidos como sustancias que se disocian en el agua para formar iones  $\text{H}_3\text{O}^+$ . Se asumió que los ácidos más fuertes, tales como el ácido sulfúrico ( $\text{H}_2\text{SO}_4$ ), se disociaban mucho más que los ácidos débiles, tales como el ácido acético ( $\text{CH}_3\text{COOH}$ ).



Según la definición de Arrhenius, las bases son sustancias que se disocian en solución acuosa para formar iones hidroxilo. Por otra parte se consideró que las bases fuertes, tales como el  $\text{NaOH}$ , se disociaban más que las débiles o que aquellas que se disuelven moderadamente, como el  $\text{Mg}(\text{OH})_2$ .



La acidez o basicidad de una solución acuosa (agua) de una sustancia se mide por la concentración de  $\text{H}_3\text{O}^+$  en dicha disolución. Este valor también permite conocer implícitamente la concentración de  $\text{OH}^-$ , ya que estas dos concentraciones están relacionadas entre sí por la constante de ionización del agua:

$$K_w = [\text{H}_3\text{O}^+][\text{OH}^-] = 1.00 \times 10^{-14} \quad (\text{a } 24^\circ\text{C})$$

## 1.12

### Ácidos y bases de Arrhenius

En las soluciones neutras la concentración de  $[\text{H}_3\text{O}^+]$  y de  $[\text{OH}^-]$  son iguales,

$$[\text{H}_3\text{O}^+] = [\text{OH}^-] = 1.0 \times 10^{-7} \text{ M} \text{ en una solución neutra}$$

Las soluciones ácidas y básicas poseen un exceso de  $[\text{H}_3\text{O}^+]$  o de  $[\text{OH}^-]$ , respectivamente.

$$\text{ácidas: } [\text{H}_3\text{O}^+] > 10^{-7} \text{ M} \text{ y } [\text{OH}^-] < 10^{-7} \text{ M}$$

$$\text{básicas: } [\text{H}_3\text{O}^+] < 10^{-7} \text{ M} \text{ y } [\text{OH}^-] > 10^{-7} \text{ M}$$

Como estas concentraciones pueden abarcar un amplio rango de valores, la acidez o basicidad de una solución normalmente se mide en escala logarítmica. El **pH** se define como el logaritmo (en base 10), cambiado de signo, de la concentración de  $\text{H}_3\text{O}^+$ .

$$\text{pH} = -\log_{10}[\text{H}_3\text{O}^+]$$

Una solución neutra tiene un pH de 7, una solución ácida tiene un pH menor que 7 y una solución básica tiene un pH mayor que 7.

### PROBLEMA 1.13

Calcule el pH de las siguientes soluciones:

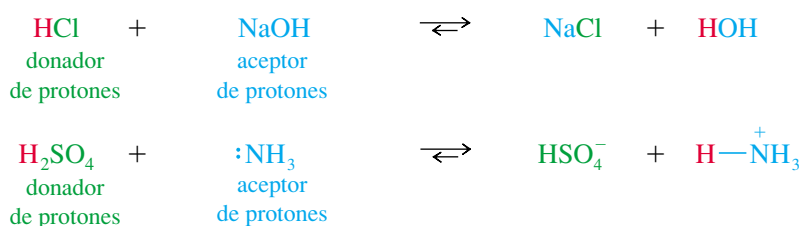
- (a) 5.00 g de HBr en 100 mL de solución acuosa.
- (b) 1.50 g de NaOH en 50 mL de solución acuosa.

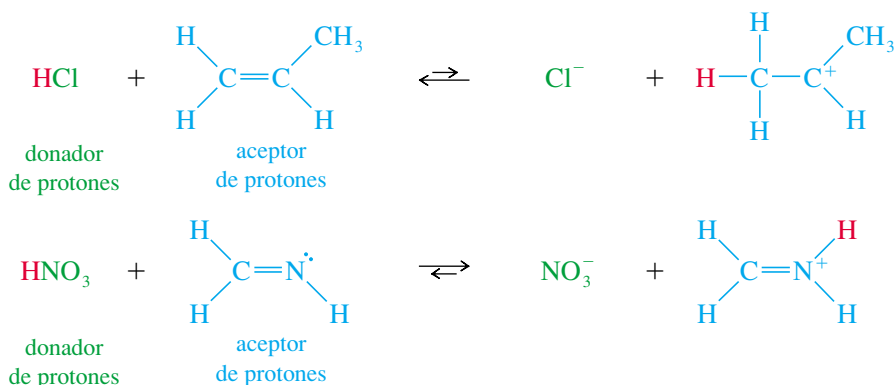
La definición de Arrhenius fue una contribución importante para poder entender muchos ácidos y muchas bases, pero no explica por qué un compuesto como el amoníaco ( $\text{NH}_3$ ) neutraliza los ácidos, a pesar de no tener un ión hidróxido en su fórmula molecular. En la Sección 1.13 se explica una teoría más versátil de ácidos y bases que incluye al amoníaco y a una variedad más amplia de ácidos y bases orgánicos.

## 1.13 Ácidos y bases de Brønsted-Lowry

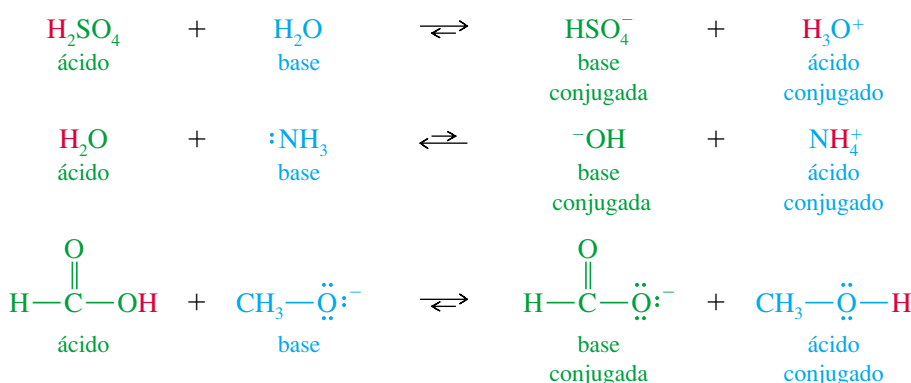
En 1923, Brønsted y Lowry definieron los ácidos y las bases teniendo en cuenta su capacidad de liberar o captar protones, respectivamente. Un **ácido de Brønsted-Lowry** es cualquier especie que puede donar un protón, y una **base de Brønsted-Lowry** es cualquier especie que puede aceptar un protón. Estas definiciones también incluyen todos los ácidos y bases de Arrhenius, ya que los compuestos que se disocian para dar  $\text{H}_3\text{O}^+$  son donadores de protones y los compuestos que se disocian para dar  $\text{OH}^-$  son aceptores de protones (el ión hidróxido acepta un protón para formar  $\text{H}_2\text{O}$ ).

Además de los ácidos y bases de Arrhenius, la definición de Brønsted-Lowry incluye también las bases que no tienen iones hidróxido, y que pueden aceptar protones. Observe los ejemplos siguientes de ácidos capaces de ceder protones a las bases. El NaOH es una base tanto si se considera la definición de Arrhenius o la de Brønsted-Lowry. Los tres ejemplos siguientes son bases de Brønsted-Lowry pero no bases de Arrhenius, ya que no tienen iones hidróxido.



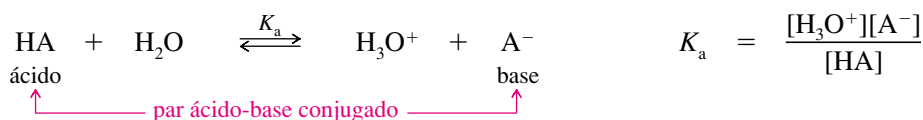


Cuando una base acepta un protón, se convierte en un ácido capaz de devolver ese protón. Cuando un ácido cede un protón, se convierte en una base capaz de aceptar de nuevo ese protón. Uno de los principios más importantes de la definición de Brønsted-Lowry es el concepto de **ácidos y bases conjugados**. Por ejemplo, el  $\text{NH}_3$  y el  $\text{NH}_4^+$  forman un par de ácido y base conjugados; el  $\text{NH}_3$  es la base, cuando acepta un protón, se transforma en el ácido conjugado,  $\text{NH}_4^+$ . Muchos compuestos (por ejemplo, el agua) pueden reaccionar como un ácido o como una base. A continuación se dan algunos ejemplos de pares ácido-base conjugados:



### 1.13A Fuerza de los ácidos

La fuerza de un ácido de Brønsted-Lowry se expresa de forma similar a la definición de Arrhenius, teniendo en cuenta su grado de ionización en agua. La reacción general de un ácido (HA) con agua es la siguiente:



A la  $K_a$  se la conoce con el nombre de *constante de disociación del ácido* y su valor indica la fuerza relativa del ácido. Cuanto más fuerte es el ácido, más se disocia, dando un valor de  $K_a$  mayor. Las constantes de disociación de un ácido varían en un intervalo amplio. Los ácidos fuertes se ionizan casi completamente en agua y sus constantes de disociación son superiores a 1. La mayoría de los ácidos orgánicos son ácidos débiles, con valores de  $K_a$  menores que  $10^{-4}$ . Muchos compuestos orgánicos son ácidos extremadamente débiles; por ejemplo, el metano y el etano tienen un carácter ácido muy débil, su  $K_a$  es inferior a  $10^{-40}$ .

Debido a este amplio margen de valores, las constantes de disociación ácida frecuentemente se expresan en escala logarítmica. El  $\text{p}K_a$  de un ácido se define de forma parecida al pH: logaritmo (en base 10), con signo negativo, de la  $K_a$ .

$$\text{p}K_a = -\log_{10} K_a$$

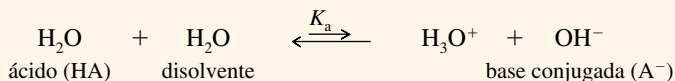


**PROBLEMA RESUELTO 1.3**

Calcule la  $K_a$  y el  $pK_a$  del agua.

**SOLUCIÓN**

El equilibrio que define la  $K_a$  del agua es:



El agua se comporta en esta disolución como ácido y como disolvente. La expresión del equilibrio es:

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]} = \frac{[\text{H}_3\text{O}^+][\text{OH}^-]}{[\text{H}_2\text{O}]}$$

Donde  $[\text{H}_3\text{O}^+][\text{OH}^-] = 1.00 \times 10^{-14}$ , constante del producto de ionización del agua.

La concentración de moléculas de  $\text{H}_2\text{O}$  en el agua simplemente es el número de moles de agua en 1 L (aproximadamente 1 kg).

$$\frac{1000 \text{ g/L}}{18 \text{ g/mol}} = 55.6 \text{ mol/L}$$

Haciendo la sustitución:

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{OH}^-]}{[\text{H}_2\text{O}]} = \frac{1.00 \times 10^{-14}}{55.6} = 1.8 \times 10^{-16} \text{ M}$$

El logaritmo de  $1.8 \times 10^{-16}$  es  $-15.7$ , por lo que el  $pK_a$  del agua es 15.7.

**SUGERENCIA  
PARA RESOLVER PROBLEMAS**

En la mayor parte de los casos, el  $pK_a$  de un ácido coincide con el valor del pH de un ácido disociado en un 50%. A un pH menor (más ácido), el ácido estará menos disociado; a un pH mayor (más básico), el ácido estará más disociado.

Los ácidos fuertes generalmente tienen valores de  $pK_a$  próximos a 0 y los ácidos débiles, como la mayoría de los ácidos orgánicos, tienen valores superiores a 4. *Los ácidos más débiles tienen valores de  $pK_a$  más elevados.* La Tabla 1.5 recoge los valores de  $K_a$  y  $pK_a$  de algunos de los compuestos inorgánicos y orgánicos más habituales. Observa que los valores de  $pK_a$  aumentan cuando los valores de  $K_a$  disminuyen.

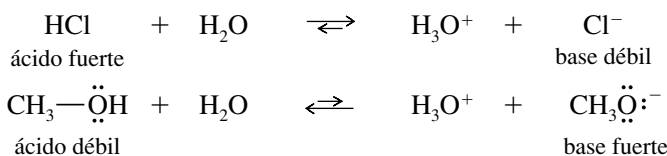
**PROBLEMA 1.14**

El amoníaco se encuentra en la Tabla 1.5 de dos formas, la forma básica y su ácido conjugado.

- Explique cómo el amoníaco puede actuar como base y como ácido. ¿Cuál de estas dos formas es más habitual en las soluciones acuosas?
- Explique por qué el agua puede actuar como ácido y como base.
- Explique por qué el metanol ( $\text{CH}_3\text{OH}$ ) puede comportarse como ácido y como base. Escriba una ecuación para la reacción del metanol con el ácido sulfúrico.

**1.13B Fuerza de las bases**

La fuerza de un ácido es inversa a la fuerza de su base conjugada. Si un ácido (HA) es fuerte, su base conjugada ( $\text{A}^-$ ) será débil, al ser estable en su forma aniónica; de lo contrario, el ácido HA no perdería fácilmente sus protones. Por lo tanto, la base conjugada de un ácido fuerte será una base débil. Por otra parte, si un ácido es débil, su conjugado es una base fuerte.

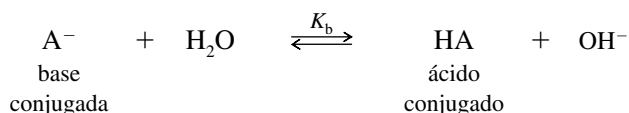


En la reacción de un ácido con una base, el equilibrio generalmente está desplazado hacia la formación de los ácidos y bases *débiles*. Por ejemplo, en las reacciones anteriores, el  $\text{H}_3\text{O}^+$  es un ácido más débil que el HCl, pero un ácido más fuerte que el  $\text{CH}_3\text{OH}$ ; esto conlleva que el  $\text{H}_2\text{O}$  sea una base más fuerte que el  $\text{Cl}^-$ , pero más débil que el  $\text{CH}_3\text{O}^-$ .

**TABLA 1.5** Fuerza relativa de algunos ácidos inorgánicos y orgánicos frecuentes, y sus bases conjugadas

	Ácido		Base conjugada	$K_a$	$pK_a$
ácidos fuertes	<b>HCl</b> ácido clorhídrico	$+ H_2O \rightleftharpoons H_3O^+ + Cl^-$	ion cloruro	$1.6 \times 10^2$	-2.2
	<b>HF</b> ácido fluorhídrico	$+ H_2O \rightleftharpoons H_3O^+ + F^-$	ion fluoruro	$6.8 \times 10^{-4}$	3.17
	$\begin{array}{c} O \\    \\ H-C-OH \end{array}$ ácido fórmico	$+ H_2O \rightleftharpoons H_3O^+ + \begin{array}{c} O \\    \\ H-C-O^- \end{array}$	ion formiato	$1.7 \times 10^{-4}$	3.76
	$\begin{array}{c} O \\    \\ CH_3-C-OH \end{array}$ ácido acético	$+ H_2O \rightleftharpoons H_3O^+ + \begin{array}{c} O \\    \\ CH_3-C-O^- \end{array}$	acetano ion	$1.8 \times 10^{-5}$	4.74
ácidos débiles	<b><math>H-C \equiv N:</math></b> ácido cianhídrico	$+ H_2O \rightleftharpoons H_3O^+ + :C \equiv N:$	ion cianuro	$6.0 \times 10^{-10}$	9.22
	<b><math>^+NH_4</math></b> ion amonio	$+ H_2O \rightleftharpoons H_3O^+ + :NH_3$	amoniaco	$5.8 \times 10^{-10}$	9.24
	<b><math>CH_3-OH</math></b> alcohol metílico	$+ H_2O \rightleftharpoons H_3O^+ + CH_3O^-$	metóxido ion	$3.2 \times 10^{-16}$	15.5
	<b><math>H_2O</math></b> agua	$+ H_2O \rightleftharpoons H_3O^+ + HO^-$	ion hidróxido	$1.8 \times 10^{-16}$	15.7
muy débil	<b><math>NH_3</math></b> amoniaco	$+ H_2O \rightleftharpoons H_3O^+ + :\ddot{N}H_2$	ion amiduro	$10^{-33}$	33
no ácido	<b><math>CH_4</math></b> metano	$+ H_2O \rightleftharpoons H_3O^+ + :\ddot{C}H_3$	anión metilo	$<10^{-40}$	$>40$

La fuerza de una base se mide de forma similar a la de los ácidos, usando la constante de equilibrio de la reacción de hidrólisis:



La constante de equilibrio ( $K_b$ ) para esta reacción se conoce con el nombre de *constante de disociación de la base* para la base  $A^-$ . Debido a que esta constante tiene un amplio rango de valores, frecuentemente se expresa en forma logarítmica. El  $pK_b$  se define como el logaritmo (en base 10), cambiado de signo, de la  $K_b$ .

$$K_b = \frac{[HA][OH^-]}{[A^-]} \quad pK_b = -\log_{10} K_b$$

Cuando se multiplica  $K_a$  por  $K_b$ , se puede apreciar cómo la acidez de un ácido está relacionada con la basicidad de su base conjugada:

Las propiedades ácido-base de muchos productos naturales son importantes de cara a su aislamiento, a su distribución en el cuerpo y a justificar sus efectos terapéuticos. Por ejemplo, la morfina (p. 2), que se aísla de las adormideras (opio), llega al cerebro como base libre, en la que el nitrógeno no está cargado. Sin embargo, son sus especies cargadas las que actúan como analgésicas.

$$(K_a)(K_b) = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]} \frac{[\text{HA}][\text{OH}^-]}{[\text{A}^-]} = [\text{H}_3\text{O}^+][\text{OH}^-] = 1.0 \times 10^{-14}$$

constante del producto de ionización del agua

$$(K_a)(K_b) = 10^{-14}$$

Aplicando logaritmos:

$$\text{p}K_a + \text{p}K_b = -\log 10^{-14} = 14$$

El producto de  $K_a$  por  $K_b$  siempre es igual a la constante del producto iónico del agua,  $10^{-14}$ . Si el valor de  $K_a$  es grande, el valor de  $K_b$  será pequeño; es decir, cuanto más fuerte es un ácido, más débil es su base conjugada. De forma similar, un valor pequeño de  $K_a$  (ácido débil) implica un valor grande de  $K_b$  (base fuerte).

Cuanto más fuerte es un ácido, más débil es su base conjugada.

Cuanto más débil es un ácido, más fuerte es su base conjugada.

Las reacciones ácido-base favorecen la formación de ácidos más débiles y/o bases más débiles.

## SUGERENCIA PARA RESOLVER PROBLEMAS

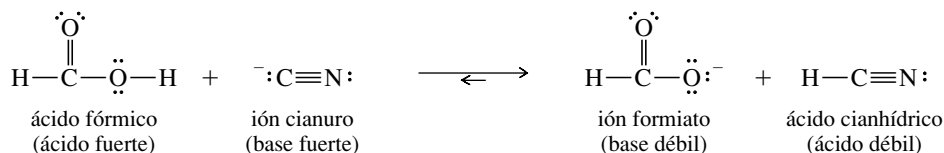
Un ácido donará un protón a la base conjugada de cualquier ácido que sea más débil (menor  $K_a$  o mayor  $\text{p}K_a$ ).

### PROBLEMA 1.15 (parcialmente resuelto)

Escriba las ecuaciones para las siguientes reacciones ácido-base. Utilice la información de la Tabla 1.5 para predecir si el equilibrio favorecerá a los reactivos o a los productos.

- |  |  |
|--|--|
| (a) $\text{HCOOH} + ^-\text{CN}$           | (b) $\text{CH}_3\text{COO}^- + \text{CH}_3\text{OH}$ |
| (c) $\text{CH}_3\text{OH} + \text{NaNH}_2$ | (d) $\text{NaOCH}_3 + \text{HCN}$                    |
| (e) $\text{HCl} + \text{H}_2\text{O}$      | (f) $\text{H}_3\text{O}^+ + \text{CH}_3\text{O}^-$   |

**Solución para (a):** el ión cianuro es la base conjugada del HCN; puede aceptar un protón del ácido fórmico:



Observando la Tabla 1.5, se aprecia que el ácido fórmico ( $\text{p}K_a = 3.76$ ) es un ácido más fuerte que el HCN ( $\text{p}K_a = 9.22$ ) y que el cianuro es una base más fuerte que el formiato. Resultan favorecidos, pues, los productos ácido y base más débiles.

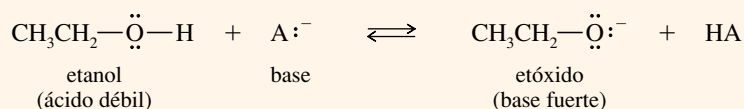
### PROBLEMA RESUELTO 1.4

Cada uno de los compuestos siguientes puede actuar como un ácido. Escriba la reacción de cada compuesto con una base general ( $\text{A}^-$ ) y la estructura de Lewis de la base conjugada que se obtiene.

- |                                       |                              |                              |
|---------------------------------------|------------------------------|------------------------------|
| (a) $\text{CH}_3\text{CH}_2\text{OH}$ | (b) $\text{CH}_3\text{NH}_2$ | (c) $\text{CH}_3\text{COOH}$ |
|---------------------------------------|------------------------------|------------------------------|

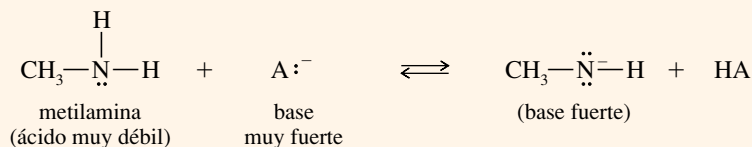
### SOLUCIÓN

- (a) El etanol ( $\text{CH}_3\text{CH}_2\text{OH}$ ) puede perder el protón del grupo  $\text{O}-\text{H}$  para formar una base conjugada que es un ión orgánico análogo al ión hidroxilo.

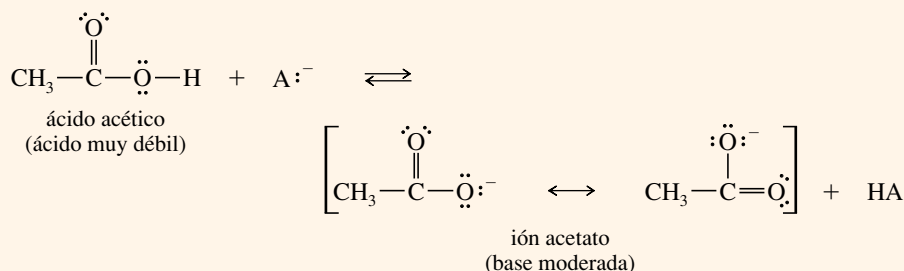


(Los protones del grupo  $\text{C}-\text{H}$  son mucho menos ácidos que los protones del grupo  $\text{O}-\text{H}$ , porque el carbono es menos electronegativo que el oxígeno y, por lo tanto, la carga negativa es menos estable en el carbono.)

- (b) La metilamina ( $\text{CH}_3\text{NH}_2$ ) es un ácido muy débil. Una base muy fuerte le puede sustraer un protón y dar lugar a una base conjugada fuerte.



- (c) El ácido acético ( $\text{CH}_3\text{COOH}$ ) es un ácido moderadamente fuerte. Su base conjugada es el ión acetato que está estabilizado por resonancia.

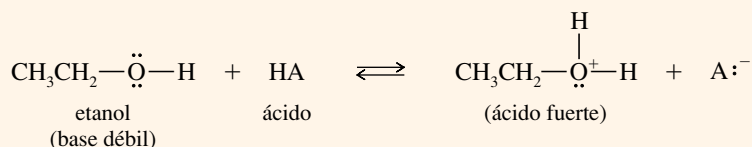


### PROBLEMA RESUELTO 1.5

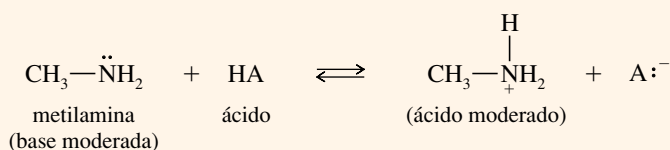
Cada uno de los compuestos del Problema resuelto 1.4 también pueden reaccionar como una base. Escriba la reacción de cada compuesto con un ácido general (HA) y las estructuras de Lewis del ácido conjugado que se obtiene.

### SOLUCIÓN

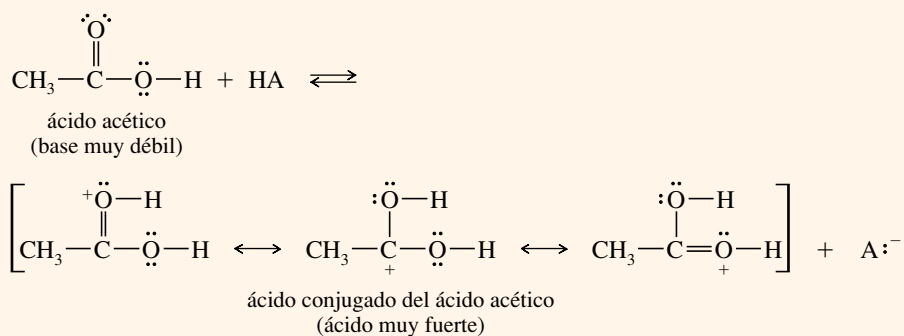
- (a) El etanol puede protonarse en su átomo de oxígeno. Observe que uno de los pares solitarios del oxígeno forma el nuevo enlace  $\text{O}-\text{H}$ .



- (b) El átomo de nitrógeno de la metilamina tiene un par de electrones que pueden enlazarse con un protón.



- (c) El ácido acético tiene electrones no enlazantes en los dos átomos de oxígeno. Cada uno de estos átomos de oxígeno podría protonarse, pero la protonación de oxígeno que forma parte del doble enlace está favorecida porque la protonación de este oxígeno da lugar a un ácido conjugado simétrico y estabilizado por resonancia.



**PROBLEMA 1.16**

El Problema resuelto 1.5(c) muestra la protonación del oxígeno con doble enlace del ácido acético. Escriba el producto obtenido de la protonación en el otro oxígeno ( $\text{—OH}$ ). Explique por qué la protonación del oxígeno con doble enlace está favorecida.

**PROBLEMA 1.17**

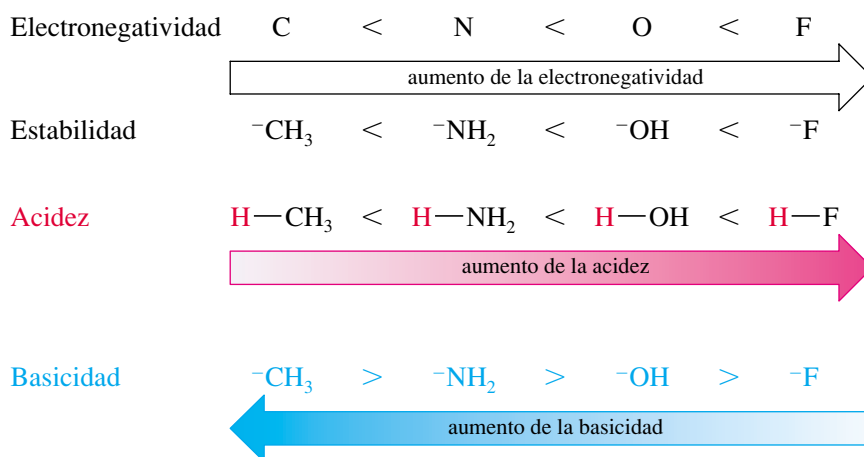
- (a) Ordene por orden decreciente de acidez el etanol, la metilamina y el ácido acético.  
 (b) Ordene por orden decreciente de basicidad el etanol, la metilamina ( $\text{p}K_b = 3.36$ ) y el ión etóxido ( $\text{CH}_3\text{CH}_2\text{O}^-$ ). En cada caso, explique las razones de este orden.

**1.13C Efectos estructurales en la acidez**

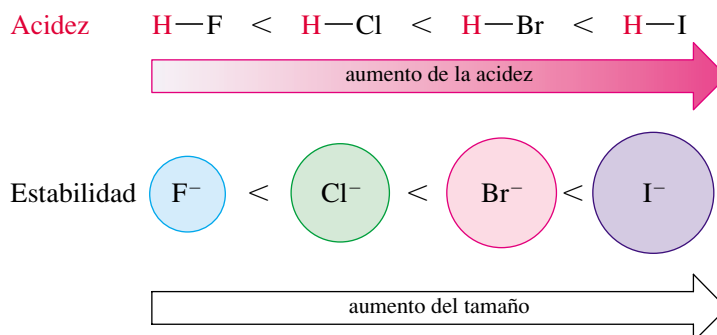
Cuando se observa una estructura, ¿cómo se puede predecir si el compuesto será un ácido fuerte o débil, o bien si no tendrá nada de carácter ácido? Según la teoría de Brønsted-Lowry, un ácido (HA) es un compuesto que ha de contener un átomo de hidrógeno que puede ser cedido como un protón. Un ácido fuerte debe formar una base conjugada estable ( $\text{A}^-$ ) después de perder el protón.

La estabilidad de la base conjugada es una buena guía para conocer la fuerza del ácido. Los aniones más estables tienden a ser bases más débiles y sus ácidos conjugados tienden a ser ácidos más fuertes. Algunos de los factores que afectan a la estabilidad de las bases conjugadas son la electronegatividad, el tamaño y la resonancia.

**Electronegatividad** Cuanto más electronegativo sea un elemento, será capaz de adquirir una carga negativa con más facilidad, lo que dará lugar a una base conjugada más estable y a un ácido fuerte. La electronegatividad aumenta de izquierda a derecha en la tabla periódica.



**Tamaño** La carga negativa de un anión es más estable cuando se distribuye sobre una región del espacio más amplia. Si se considera una columna de la tabla periódica, la acidez aumenta hacia abajo, a medida que el tamaño de los elementos aumenta.



**Estabilización por resonancia** La carga negativa de una base conjugada puede estar deslocalizada entre dos o más átomos, y estabilizada por resonancia. Dependiendo de la electronegatividad que tengan esos átomos y de cómo se comparta esa carga, la deslocalización por resonancia con frecuencia es el efecto dominante que ayuda a la estabilización del anión. Observe las bases conjugadas siguientes:

Base conjugada	Ácido	pK <sub>a</sub>
$\text{CH}_3\text{CH}_2-\ddot{\text{O}}:^-$ ión etóxido	$\text{CH}_3\text{CH}_2-\text{OH}$ etanol	15.9 (ácido débil)
$\left[ \text{CH}_3-\overset{\text{O}}{\underset{\cdot\cdot}{\parallel}}\text{C}-\ddot{\text{O}}:^- \longleftrightarrow \text{CH}_3-\overset{\cdot\cdot}{\underset{\cdot\cdot}{\parallel}}\text{C}=\ddot{\text{O}}:^- \right]$ ión acetato	$\text{CH}_3-\overset{\text{O}}{\parallel}\text{C}-\text{OH}$ ácido acético	4.74 (ácido moderado)
$\left[ \text{CH}_3-\overset{\text{O}}{\underset{\cdot\cdot}{\parallel}}\text{S}-\ddot{\text{O}}:^- \longleftrightarrow \text{CH}_3-\overset{\cdot\cdot}{\underset{\cdot\cdot}{\parallel}}\text{S}=\ddot{\text{O}}:^- \longleftrightarrow \text{CH}_3-\overset{\cdot\cdot}{\underset{\cdot\cdot}{\parallel}}\text{S}=\ddot{\text{O}}:^- \right]$ ión metanosulfonato	$\text{CH}_3-\overset{\text{O}}{\parallel}\text{S}-\text{OH}$ ácido metanosulfónico	-1.2 (ácido fuerte)

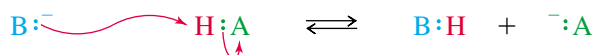
El ión etóxido es el más fuerte de las tres bases anteriores. El etóxido tiene una carga negativa localizada en un átomo de oxígeno; el ión acetato tiene una carga negativa compartida por dos átomos de oxígeno y el ión metanosulfonato tiene una carga negativa extendida sobre tres átomos de oxígeno. Los valores de los pK<sub>a</sub> de los ácidos conjugados de esos aniones muestran que los ácidos son más fuertes si su desprotonación da lugar a bases conjugadas estabilizadas por resonancia.

### PROBLEMA 1.18

Escriba las ecuaciones correspondientes a las reacciones ácido-base siguientes. Señale los ácidos y bases conjugados y justifique, si es el caso, su estabilización por resonancia escribiendo las posibles formas resonantes. Prediga si el equilibrio está desplazado hacia los reactivos o hacia los productos.

- (a)  $\text{CH}_3\text{CH}_2\text{OH} + \text{CH}_3\text{NH}^-$       (b)  $\text{CH}_3\text{CH}_2\text{COOH} + \text{CH}_3\text{NHCH}_3$   
 (c)  $\text{CH}_3\text{OH} + \text{H}_2\text{SO}_4$       (d)  $\text{NaOH} + \text{H}_2\text{S}$   
 (e)  $\text{CH}_3\text{NH}_3^+ + \text{CH}_3\text{O}^-$       (f)  $\text{CH}_3\text{O}^- + \text{CH}_3\text{COOH}$   
 (g)  $\text{CH}_3\text{SO}_3^- + \text{CH}_3\text{COOH}$

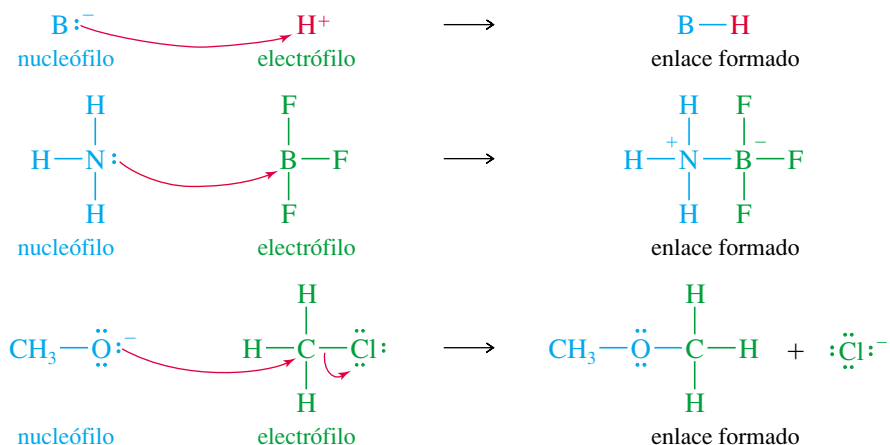
La definición de Brönsted-Lowry de ácidos y bases depende de la transferencia de un protón del ácido a la base. La base utiliza un par de electrones no enlazantes para formar un enlace con el protón. G. N. Lewis pensó que esta clase de reacciones no necesitaba obligatoriamente un protón para tener lugar. Una base podría usar su par solitario de electrones para enlazarse a algún otro átomo deficiente en electrones. En efecto, puede haber reacciones ácido-base desde el punto de vista de los *enlaces* que se forman y rompen, sin necesidad de que se transfiera un protón. La siguiente reacción muestra la transferencia del protón haciendo hincapié en los enlaces que se forman y que se rompen. Los químicos orgánicos utilizan de forma rutinaria flechas curvadas para mostrar el movimiento de los electrones que participan,



Las **bases de Lewis** son especies con electrones no enlazantes que pueden ser cedidos para formar nuevos enlaces. Los **ácidos de Lewis** son especies que pueden aceptar esos pares de electrones para formar nuevos enlaces. Debido a que un ácido de Lewis *acepta* un par de electrones, se le conoce como **electrófilo**, palabra derivada del griego, que significa «amante de electrones». A la base de Lewis se le llama **nucleófilo**, o «amante de los núcleos», ya que cede electrones a un núcleo que tenga un orbital vacío (o prácticamente vacío). En este libro, a veces se usan caracteres coloreados para enfatizar: azul para los nucleófilos, verde para los electrófilos y ocasionalmente rojo para los protones ácidos.

## 1.14 Ácidos y bases de Lewis

Las definiciones ácido-base de Lewis incluyen reacciones que no tienen ninguna relación con los protones. A continuación se muestran algunos ejemplos de reacciones ácido-base de Lewis. Observe que los ácidos y las bases de Brønsted-Lowry también están incluidos dentro de la definición de Lewis, siendo el protón un electrófilo. Las flechas curvadas (rojas) se usan para mostrar el movimiento de los electrones, generalmente desde el nucleófilo al electrófilo.

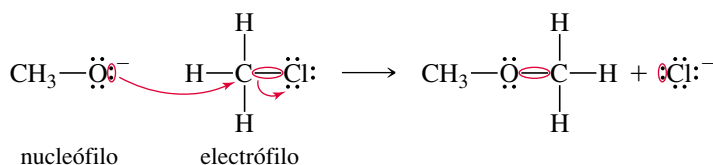


Algunos de los términos asociados con los ácidos y bases poseen significados específicos en química orgánica. Cuando un químico orgánico utiliza el término *base*, normalmente quiere decir «aceptor de protones» (una base de Brønsted-Lowry). De manera similar, el término *ácido* normalmente implica a un protón ácido (un ácido de Brønsted-Lowry). Cuando una reacción ácido-base implica la formación de un enlace con otro elemento (especialmente carbono), un químico orgánico denomina al donador de electrones *nucleófilo* (base de Lewis) y al aceptor de electrones, *electrófilo* (ácido de Lewis).

Las **flechas curvadas** se utilizan para mostrar el movimiento de un par de electrones *desde el donador de electrones al aceptor de electrones*. El movimiento de cada par de electrones implicado en formar o romper enlaces se indica por sus propias flechas separadas, como se muestra en las reacciones anteriores. En este libro, estas flechas curvadas se dibujan siempre en rojo. En la reacción anterior del  $CH_3O^-$  con  $CH_3Cl$ , una flecha curvada muestra el par solitario del oxígeno formando un enlace con el carbono; otra flecha curvada muestra que el par enlazante del  $C-Cl$  se separa del átomo de carbono y se transforma en un par solitario formando el ión  $Cl^-$ .

## SUGERENCIA PARA RESOLVER PROBLEMAS

Utilice una flecha curvada para cada par de electrones que participen en la reacción.



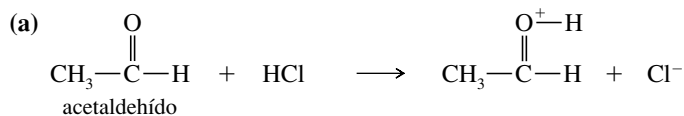
La flecha curvada se usa universalmente para seguir el camino del movimiento de los electrones en las reacciones; en este libro también se ha utilizado (en la Sección 1.9, por ejemplo) para seguir el movimiento de los electrones en las estructuras de resonancia, con objeto de representar el supuesto «flujo electrónico» cuando se pasaba de una estructura de resonancia a otra. Recuerde que los electrones no «fluyen» en las estructuras de resonancia, simplemente están deslocalizados. Este formalismo de las flechas nos ayuda, sin embargo, a comprender la interconversión entre las formas resonantes. Estas flechas curvadas se usan constantemente para seguir el camino de los electrones, tanto en el cambio de reactivos a productos como cuando imaginamos nuevas estructuras resonantes adicionales de un híbrido de resonancia.

### PROBLEMA 1.19 (parcialmente resuelto)

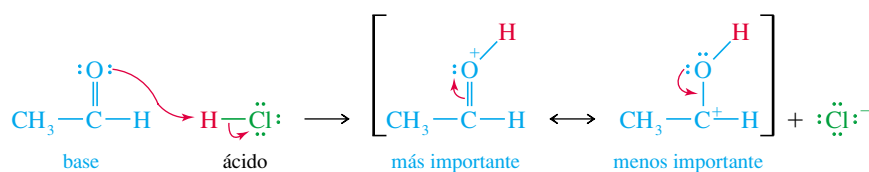
En las siguientes reacciones ácido-base:

- (1) Determine qué especies actúan como ácidos y cuáles como bases.
- (2) Utilice las flechas curvadas para mostrar el movimiento de los pares de electrones de las reacciones, así como el movimiento imaginario de electrones en los híbridos de resonancia de los productos.

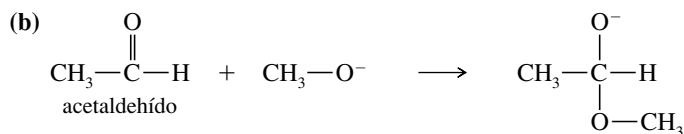
(3) Indique qué reacciones son las más apropiadas para poderlas incluir dentro de las reacciones ácido-base de Brønsted-Lowry.



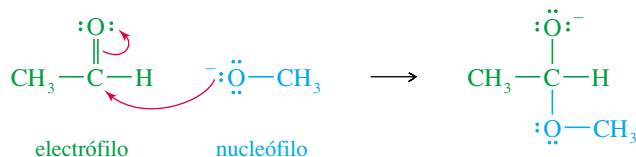
En esta reacción hay transferencia del protón del HCl al grupo C=O del acetaldehído, por tanto, es una reacción ácido-base de Brønsted-Lowry, donde el HCl actúa como ácido (donador de protones) y el acetaldehído actúa como base (aceptor de protones). Antes de dibujar una flecha curvada, recuerde que las flechas deben mostrar el movimiento de los electrones *desde* el donador del par de electrones (la base) *hasta* el aceptor del par de electrones (el ácido). Una flecha debe ir *desde* los electrones no enlazantes del acetaldehído *hasta* el átomo de hidrógeno del HCl y el enlace del ácido clorhídrico se ha de romper, con la formación del ión cloruro que ha captado los electrones del enlace H—Cl. Dibujar las flechas es fácil después de haber representado correctamente estructuras de Lewis de todos los reactivos y productos.



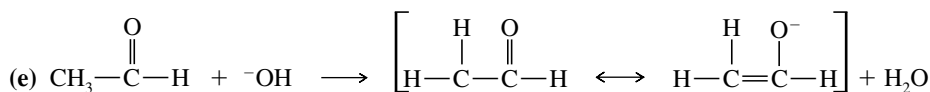
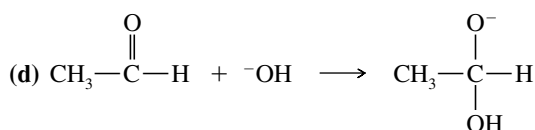
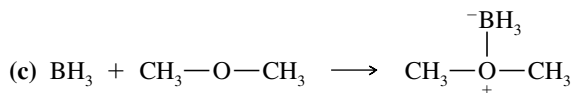
Las formas de resonancia del producto muestran que un par de electrones puede moverse entre el átomo de oxígeno y el enlace pi del C=O. La carga positiva está deslocalizada sobre los átomos de carbono y de oxígeno, con la mayor parte de la carga positiva sobre el oxígeno, ya que todos los octetos están completos en esa estructura de resonancia.



En este caso, ningún protón se ha transferido, por lo que no es una reacción ácido-base de Brønsted-Lowry. En su lugar, se ha formado un enlace entre el átomo de carbono del grupo C=O y el átomo de oxígeno del grupo CH<sub>3</sub>—O<sup>−</sup>. Dibujar las estructuras de Lewis ayuda a ver que el grupo CH<sub>3</sub>—O<sup>−</sup> (el nucleófilo en esta reacción) cede los electrones para formar el nuevo enlace con el acetaldehído (el electrófilo). Este resultado concuerda con la intuición de que un ión cargado negativamente es probablemente rico en electrones y por tanto un donador de electrones.



Observe que el acetaldehído actúa como nucleófilo (base) en (a) y como electrófilo en (b). Como la mayoría de los compuestos orgánicos, el acetaldehído puede ser tanto un ácido como una base. Actúa como una base si se le añade un ácido lo suficientemente fuerte para que ceda un par de electrones o capte un protón.



## SUGERENCIA PARA RESOLVER PROBLEMAS

Las flechas curvadas se utilizan en los mecanismos para mostrar el *flujo de electrones* y no el movimiento de los átomos. Estas flechas curvadas se usarán constantemente a lo largo de este curso.



## Glosario del Capítulo 1

Cada capítulo finaliza con un glosario que recoge los términos nuevos más importantes del capítulo. Estos glosarios son más que un diccionario en el que se buscan términos desconocidos conforme se los vaya encontrando (el índice sirve para este propósito). El glosario es una de las herramientas para revisar el capítulo, se puede leer cuidadosamente para saber si se entienden y se recuerdan todos los términos químicos mencionados. Cualquier concepto que no resulte familiar debería ser revisado volviendo a la página que aparece numerada en el mismo.

**Ácido conjugado** El ácido que resulta de la protonación de una base. (p. 23)

**Ácido de Lewis, base de Lewis.** Véase ácidos y bases.

**Ácidos y bases** (pp. 21-31)

(definiciones de Arrhenius)

**Ácido:** se disocia en agua para dar  $\text{H}_3\text{O}^+$ .

**Base:** se disocia en agua para dar  $\text{OH}^-$ .

(definiciones de Brønsted-Lowry)

**Ácido:** donador de protones.

**Base:** aceptor de protones.

(definiciones de Lewis)

**Ácido:** aceptor de un par de electrones (electrófilo).

**Base:** donador de un par de electrones (nucleófilo).

**Base conjugada** La base que resulta de la pérdida de un protón de un ácido. (p. 23)

**Cargas formales** Método para hacer un seguimiento de las cargas, el cual permite mostrar qué carga habría en una determinada estructura de Lewis. (p. 11)

**Densidad electrónica** Probabilidad relativa de encontrar un electrón en una cierta región del espacio. (p. 3)

**Electrófilo** Aceptor de un par de electrones. (p. 29)

**Electronegatividad** Medida de la capacidad de un elemento para atraer electrones. Los elementos con electronegatividades más altas atraen a los electrones con más fuerza. (p. 10)

**Electrones de valencia** Electrones que se encuentran en la capa externa más alejada del núcleo. (p. 6)

**Electrones no enlazantes** Electrones de valencia que no se utilizan en el enlace. A un par de electrones no enlazantes con frecuencia se le denomina **par solitario**. (p. 7)

**Enlace covalente** Enlace que se forma por la compartición de electrones en la región que hay entre dos núcleos. (p. 7)

**Enlace sencillo:** enlace covalente en el que se comparte un par de electrones. (p. 8)

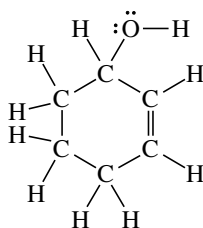
**Enlace doble:** enlace covalente en el que se comparte dos pares de electrones. (p. 8)

**Enlace triple:** enlace covalente en el que se comparte tres pares de electrones. (p. 8)

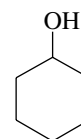
**Enlace covalente polar** Enlace covalente en el que los electrones se comparten de forma desigual. Cuando los electrones están igualmente compartidos se llama **enlace covalente no polar**. (p. 9)

**Enlace iónico** Enlace que se produce por la atracción de iones que tienen carga opuesta. El enlace iónico normalmente da lugar a la formación de una gran estructura cristalina en tres dimensiones. (p. 7)

**Estructura de Lewis** Fórmula estructural que muestra todos los electrones de valencia, con los enlaces simbolizados por líneas (—) o por pares de puntos, y los electrones no enlazantes simbolizados por puntos. (p. 7)



estructura de Lewis del 2-ciclohexenol



2-ciclohexenol  
fórmula lineoangular equivalente

**Flechas curvadas** El dibujar flechas curvadas es un método que se utiliza para seguir el camino de los electrones cuando se mueven desde el nucleófilo al electrófilo (o dentro de una molécula) durante el transcurso de una reacción. (p. 30)

**Fórmula empírica** Relación numérica de los átomos en un compuesto. (p. 20). Véase también **fórmula molecular**.

**Fórmula lineoangular (estructura esquelética o de barras)** Fórmula estructural con enlaces representados por líneas; los átomos de carbono son los puntos de encuentro entre dos líneas o el final de la línea cuando está en el extremo de la cadena. Los átomos de nitrógeno, de oxígeno y los halógenos se representan, pero los átomos de hidrógeno no. Se supone que cada átomo de carbono tiene los hidrógenos suficientes para que en total tenga cuatro enlaces. (p. 19)

**Fórmula molecular** Número de átomos de cada elemento que forman parte de una molécula de un compuesto. La **fórmula empírica** simplemente da la relación de los átomos de los diferentes elementos. Por ejemplo, la fórmula molecular de la glucosa es  $C_6H_{12}O_6$ ; su fórmula empírica es  $CH_2O$ . Ni la fórmula empírica ni la fórmula molecular dan información estructural. (p. 4)

**Fórmulas estructurales** Una **fórmula estructural completa** (tal como una estructura de Lewis) muestra todos los átomos y enlaces en la molécula. Una **fórmula estructural condensada** muestra cada átomo central y los átomos con los que está enlazado. Una **fórmula lineoangular** supone que hay un átomo de carbono donde dos líneas se encuentren, o donde la línea comience o termine. Véanse los ejemplos de la Sección 1.10. (p. 17)

**Híbrido de resonancia** Molécula o ión para el cual se pueden representar dos o más estructuras de Lewis válidas, diferenciándose solamente en la posición de los electrones de valencia. Estas estructuras de Lewis se conocen como **formas de resonancia** o **estructuras de resonancia**. Las formas de resonancia individuales no existen, pero se puede estimar sus energías relativas. A las estructuras más importantes (de energía más baja) se las conoce como **contribuyentes mayores**, y a las estructuras menos importantes (energía más alta), como **contribuyentes menores**. Cuando una carga se reparte entre dos o más átomos por resonancia, se dice que está **deslocalizada** y que la molécula está **estabilizada por resonancia**. (pp. 13-16)

**Isótopos** Átomos con el mismo número de protones pero diferente número de neutrones. Átomos del mismo elemento pero con diferentes masas atómicas. (p. 3)

**Mapa de potencial electrostático (MPE)** Representación molecular calculada por computador que utiliza colores para mostrar la distribución de carga en una molécula. En la mayoría de los casos, el MPE utiliza el color rojo para indicar las regiones ricas en electrones (potencial electrostático más negativo) y azul para indicar las regiones pobres en electrones (potencial electrostático más positivo). Los colores intermedios naranja, amarillo y verde indican regiones con potenciales electrostáticos intermedios. (p. 10)

**Momento dipolar ( $\mu$ )** Medida de la polaridad de un enlace (o una molécula), proporcional al producto de la separación de cargas por la longitud de enlace. (p. 10)

**Nodo** Región de un orbital con densidad electrónica cero. (p. 4)

**Nucleófilo** Donador de par de electrones (base de Lewis). (p. 29)

**Orbital** Estado de energía permitida para un electrón que rodea a un núcleo; función de probabilidad que define la distribución de la densidad electrónica en el espacio. El *principio de exclusión de Pauli* afirma que un orbital sólo puede ser ocupado por dos electrones, como máximo, si los espines de éstos están apareados. (p. 3)

**Orbitales degenerados** Orbitales con energías idénticas. (p. 4)

**Par solitario** Par de electrones no enlazantes. (p. 7)

**pH** Medida de la acidez de una solución, definido como el logaritmo (en base 10), cambiado de signo, de la concentración de  $H_3O^+$ .  $pH = -\log_{10}[H_3O^+]$ . (p. 22)

**Plano nodal** Región plana (plano) del espacio con densidad electrónica cero. (p. 4)

**Química orgánica** Definición nueva: química de los compuestos de carbono. Definición antigua: estudio de los compuestos derivados de los organismos vivos y sus productos naturales. (p. 1)

**Regla de Hund** Cuando hay dos orbitales o más con la misma energía (orbitales degenerados) vacíos, la configuración de energía más baja se consigue colocando los electrones en orbitales diferentes (con espines paralelos), mejor que colocándolos apareados en el mismo orbital. (p. 6)

**Regla del octeto** Los átomos generalmente se enlazan para que sus capas de valencia se completen con electrones (configuración de gas noble). Para los elementos de la segunda fila de la tabla periódica, esta configuración tiene ocho electrones de valencia. (p. 6)

**Valencia** Número de enlaces que normalmente forma un átomo. (p. 9)

**Vitalismo** Creencia en que la síntesis de compuestos orgánicos requiere la presencia de una «fuerza vital». (p. 1)

### Pautas esenciales para resolver los problemas del Capítulo 1

1. Escribir e interpretar las fórmulas estructurales de Lewis, condensadas y lineoangulares. Indicar qué átomos tienen cargas formales.
2. Escribir formas de resonancia y usarlas para predecir la estabilidad.
3. Calcular fórmulas empíricas y moleculares de composiciones elementales.
4. Predecir la acidez y la basicidad relativa basada en la estructura, en el enlace y en la resonancia de los pares ácido-base conjugados.
5. Calcular, usar e interpretar los valores de  $K_a$  y  $pK_a$ .
6. Identificar nucleófilos (bases de Lewis) y electrófilos (ácidos de Lewis) y escribir ecuaciones de reacciones ácido-base de Lewis utilizando flechas curvadas para mostrar el flujo de los electrones.

## Problemas

Es fácil engañarse a uno mismo pensando que se entiende la química orgánica cuando realmente no se entiende. Según se van leyendo a lo largo de este libro, todos los conceptos y las ideas pueden tener sentido, pero todavía no se ha aprendido a combinar y a usar esos conceptos e ideas. Un examen es un trance duro para darse cuenta de que realmente no se han entendido los contenidos.

La mejor forma de aprender química orgánica es aplicarla. Por supuesto se necesita leer y releer todo el material del capítulo, pero este nivel de entendimiento es justamente el comienzo. Se proponen problemas para poder trabajar con las ideas, aplicándolas a nuevos compuestos y reacciones que no se han visto con anterioridad. Al resolver problemas, uno se ve obligado a utilizar los conceptos y a entender lo que antes no se había comprendido, también se aumenta el nivel de autoestima y de habilidad para realizar los exámenes.

En cada capítulo se incluyen varias clases de problemas. Hay problemas dentro de los capítulos, que se introducen como ejemplos y explican cómo se han de resolver. Se ha de realizar ese tipo de problemas según se vaya leyendo el capítulo para asegurarse de que se han entendido los conceptos. Las soluciones de muchos de estos problemas se encuentran al final de libro. Los Problemas del final de cada capítulo proporcionan una experiencia adicional en el uso de los conceptos y obligan a pensar con detenimiento sobre las ideas expuestas en el texto. Para algunos de estos problemas se incluyen soluciones breves al final del libro, sin embargo, se pueden encontrar soluciones más detalladas de los mismos en el *Manual de Soluciones*.

Estudiar química orgánica sin resolver problemas es como lanzarse al aire sin paracaídas. Al principio parece divertido, pero después puede resultar duro para aquellos que carezcan de preparación.

**1.20** Defina y ponga un ejemplo para cada término:

- |                                    |                            |                               |
|------------------------------------|----------------------------|-------------------------------|
| (a) isótopos                       | (b) orbital                | (c) nodo                      |
| (d) orbitales degenerados          | (e) electrones de valencia | (f) enlace iónico             |
| (g) enlace covalente               | (h) estructura de Lewis    | (i) electrones no enlazantes  |
| (j) enlace sencillo                | (k) enlace doble           | (l) enlace triple             |
| (m) enlace polar                   | (n) cargas formales        | (o) formas de resonancia      |
| (p) fórmula molecular              | (q) fórmula empírica       | (r) ácido y base de Arrhenius |
| (s) ácido y base de Brønsted-Lowry | (t) ácido y base de Lewis  | (u) electrófilo               |
| (v) nucleófilo                     |                            |                               |

**1.21** Nombre el elemento que corresponda a cada configuración electrónica.

- (a)  $1s^2 2s^2 2p^2$       (b)  $1s^2 2s^2 2p^4$       (c)  $1s^2 2s^2 2p^6 3s^2 3p^3$       (d)  $1s^2 2s^2 2p^6 3s^2 3p^5$

**1.22** Hay una pequeña sección de la tabla periódica que se debe conocer en química orgánica. Escriba de memoria esta parte, realizando los siguientes pasos:

- (a) Haga una lista, de memoria, de los elementos de las dos primeras filas de la tabla periódica, junto con su número de electrones de valencia.  
 (b) Use esta lista para construir las dos primeras filas de la tabla periódica.  
 (c) Los compuestos orgánicos a veces contienen azufre, fósforo, cloro, bromo y yodo. Añada estos elementos a la tabla periódica.

**1.23** Para cada compuesto, diga si el enlace es covalente, iónico, o intermedio entre covalente e iónico.

- (a) NaCl      (b) NaOH      (c)  $\text{CH}_3\text{Li}$       (d)  $\text{CH}_2\text{Cl}_2$       (e)  $\text{NaOCH}_3$       (f)  $\text{HCO}_2\text{Na}$       (g)  $\text{CF}_4$

**1.24** (a) El  $\text{PCl}_3$  y el  $\text{PCl}_5$  son compuestos estables. Escriba la estructura de Lewis para los dos compuestos.

- (b) El  $\text{NCl}_3$  es un compuesto conocido, pero todos los intentos de sintetizar el  $\text{NCl}_5$  han fracasado. Escriba las estructuras de Lewis para el  $\text{NCl}_3$  y una hipotética para el  $\text{NCl}_5$ , y explique por qué el  $\text{NCl}_5$  es una estructura improbable.

**1.25** Escriba una estructura de Lewis para cada una de las especies.

- (a)  $\text{N}_2\text{H}_4$       (b)  $\text{N}_2\text{H}_2$       (c)  $(\text{CH}_3)_4\text{NCl}$       (d)  $\text{CH}_3\text{CN}$       (e)  $\text{CH}_3\text{CHO}$       (f)  $\text{CH}_3\text{S}(\text{O})\text{CH}_3$   
 (g)  $\text{H}_2\text{SO}_4$       (h)  $\text{CH}_3\text{NCO}$       (i)  $\text{CH}_3\text{OSO}_2\text{OCH}_3$       (j)  $\text{CH}_3\text{C}(\text{NH})\text{CH}_3$       (k)  $(\text{CH}_3)_3\text{CNO}$

**1.26** Escriba una estructura de Lewis para cada compuesto. Incluya todos los pares de electrones no enlazantes.

- (a)  $\text{CH}_3\text{CHCHCH}_2\text{CHCHCOOH}$       (b)  $\text{NCCH}_2\text{COCH}_2\text{CHO}$   
 (c)  $\text{CH}_2\text{CHCH}(\text{OH})\text{CH}_2\text{CO}_2\text{H}$       (d)  $\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{C}(\text{CH}_2\text{CH}_3)_2\text{CHO}$

**1.27** Escriba la fórmula lineoangular de todos los compuestos del Problema 1.26.

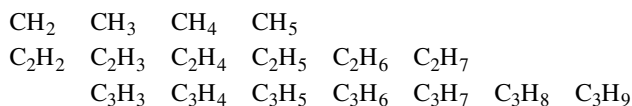
**1.28** Escriba las estructuras de Lewis para:

- (a) dos compuestos de fórmula  $\text{C}_4\text{H}_{10}$       (b) dos compuestos de fórmula  $\text{C}_2\text{H}_7\text{N}$   
 (c) dos compuestos de fórmula  $\text{C}_3\text{H}_8\text{O}_2$       (d) dos compuestos de fórmula  $\text{C}_2\text{H}_4\text{O}$

**1.29** Represente una fórmula estructural completa y una fórmula estructural condensada para:

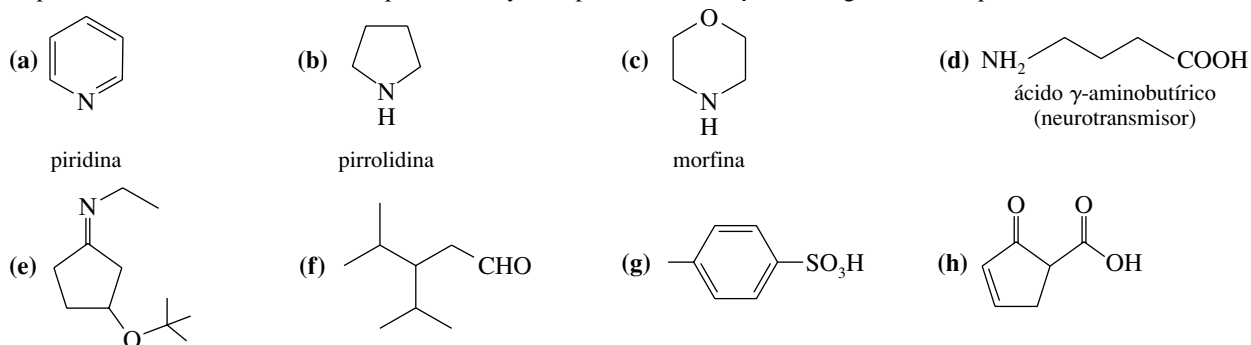
- (a) tres compuestos de fórmula  $\text{C}_3\text{H}_8\text{O}$       (b) cinco compuestos de fórmula  $\text{C}_3\text{H}_6\text{O}$

**1.30** Alguna de las siguientes fórmulas moleculares corresponde a compuestos estables. Represente, cuando sea posible, una estructura estable para cada fórmula.



Proponga una regla general que dé el número de átomos de hidrógeno en los hidrocarburos estables.

1.31 Represente estructuras de Lewis completas, incluyendo pares solitarios, para los siguientes compuestos:



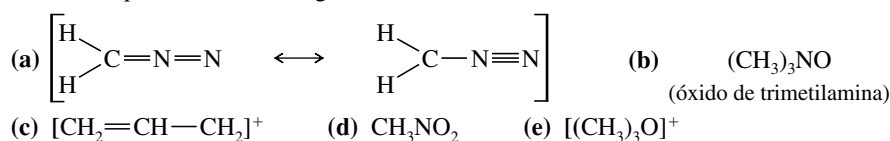
1.32 Escriba la fórmula molecular de todos los compuestos del Problema 1.31.

1.33 Un compuesto X, aislado de la lanolina (grasa de la lana de oveja), tiene un fuerte aroma a calcetines sucios sudados. Un análisis cuidadoso mostró que el compuesto X contenía un 62.0% de carbono y un 10.4% de hidrógeno. No se encontró nitrógeno ni halógenos.

- (a) Escriba la fórmula empírica del compuesto X.  
 (b) La determinación del peso molecular mostró que el compuesto X tenía un peso molecular aproximadamente igual a 117; encuentre la fórmula molecular del compuesto X.  
 (c) Hay muchas estructuras posibles que tienen esa fórmula molecular. Represente las fórmulas estructurales completas de cuatro de ellas.

1.34 Para cada una de las siguientes estructuras:

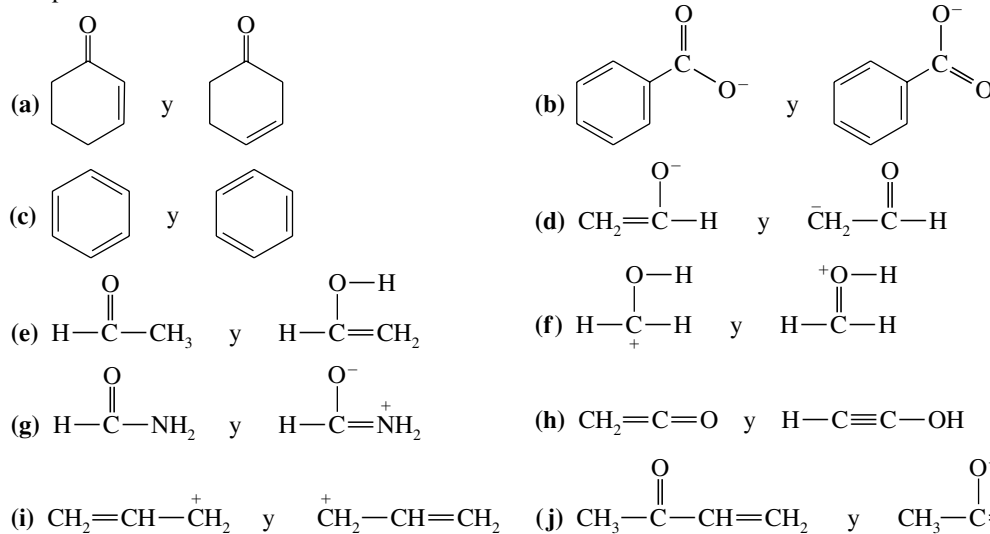
- (1) Represente una estructura de Lewis, poniendo también los electrones no enlazantes.  
 (2) Calcule la carga formal de todos los átomos excepto del hidrógeno. Todos son eléctricamente neutros excepto aquellos en los que se indica su carga.



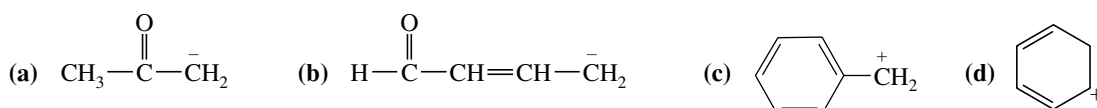
1.35 (1) Teniendo en cuenta la electronegatividad, establezca la dirección de los momentos dipolares de los siguientes enlaces.  
 (2) En cada caso, prediga si el momento dipolar es relativamente grande o pequeño.

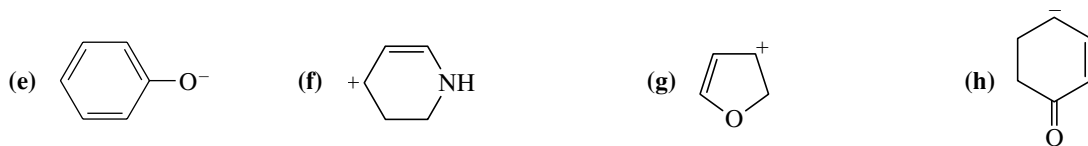
- (a)  $\text{C}-\text{Cl}$  (b)  $\text{C}-\text{H}$  (c)  $\text{C}-\text{Li}$  (d)  $\text{C}-\text{N}$  (e)  $\text{C}-\text{O}$   
 (f)  $\text{C}-\text{B}$  (g)  $\text{C}-\text{Mg}$  (h)  $\text{N}-\text{H}$  (i)  $\text{O}-\text{H}$  (j)  $\text{C}-\text{Br}$

1.36 Determine si los siguientes pares de estructuras son diferentes compuestos o solamente formas de resonancia del mismo compuesto.



1.37 Represente las formas de resonancia importantes para mostrar la deslocalización de cargas en los iones siguientes:





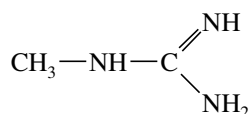
1.38

- (a) Represente las formas de resonancia para el  $\text{SO}_2$  (conectividad  $\text{O}-\text{S}-\text{O}$ ).  
 (b) Represente las formas de resonancia para el ozono (conectividad  $\text{O}-\text{O}-\text{O}$ ).  
 (c) El dióxido de azufre tiene una forma de resonancia más que el ozono, explique por qué esa estructura no es posible para el ozono.

\*1.39

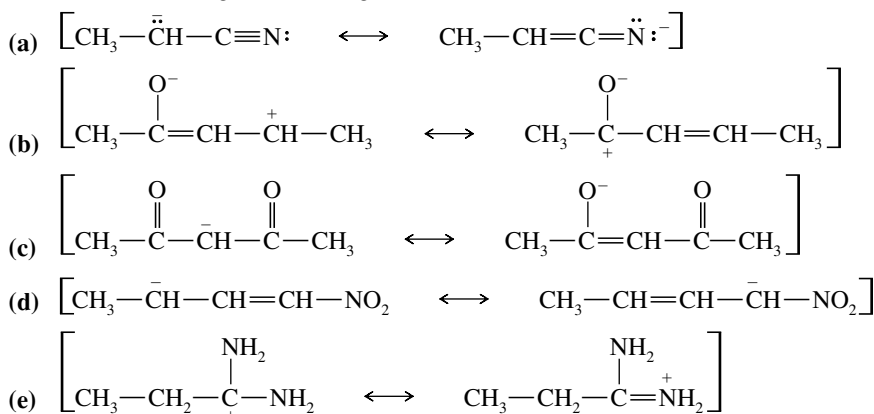
El compuesto siguiente puede protonarse en cualquiera de los átomos de nitrógeno, no obstante, uno de esos nitrógenos es mucho más básico que los otros.

- (a) Represente las formas de resonancia importantes de los productos de protonación de cada uno de los tres átomos de nitrógeno.  
 (b) Determine qué átomo de nitrógeno es el más básico.



1.40

En los siguientes apartados de formas de resonancia, señale los contribuyentes mayor y menor, y diga qué estructuras tienen la misma energía. Si falta alguna forma de resonancia, añádala.



1.41

Para cada par de iones, determine cuál es más estable. Use formas de resonancia para explicar las respuestas.

- (a)  $\text{CH}_3-\overset{+}{\text{CH}}-\text{CH}_3$  o  $\text{CH}_3-\overset{+}{\text{CH}}-\text{OCH}_3$   
 (b)  $\text{CH}_2=\text{CH}-\overset{+}{\text{CH}}-\text{CH}_3$  o  $\text{CH}_2=\text{CH}-\text{CH}_2-\overset{+}{\text{CH}}_2$   
 (c)  $\overset{-}{\text{CH}}_2-\text{CH}_3$  o  $\overset{-}{\text{CH}}_2-\text{C}\equiv\text{N}:$



1.42

Ordene las siguientes especies por orden creciente de acidez, explicando las razones de este ordenamiento.



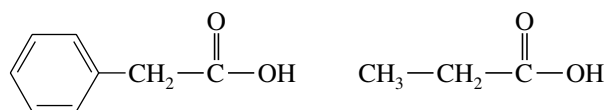
1.43

Ordene las siguientes especies por orden creciente de basicidad, explicando las razones de este ordenamiento.



1.44

La  $K_a$  del ácido fenilacético es  $5.2 \times 10^{-5}$  y el  $pK_a$  del ácido propiónico es 4.87.

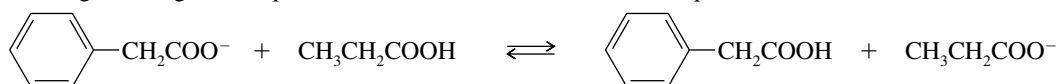


ácido fenilacético,  $K_a = 5.2 \times 10^{-5}$       ácido propiónico,  $pK_a = 4.87$

- (a) Calcule el  $pK_a$  del ácido fenilacético y la  $K_a$  del ácido propiónico.

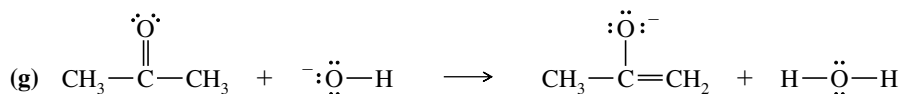
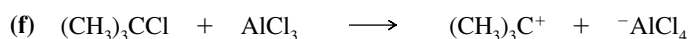
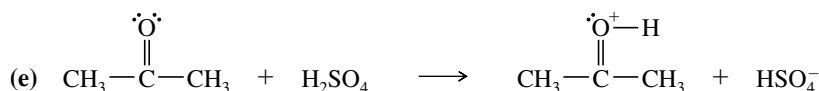
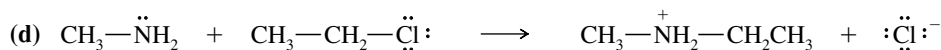
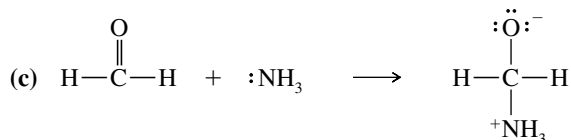
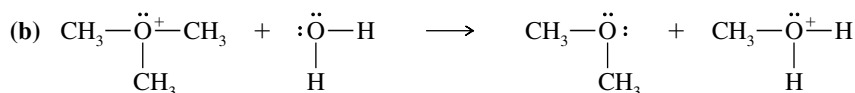
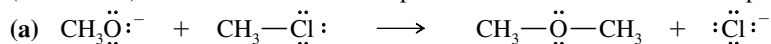
(b) ¿Cuál de los dos ácidos es el más fuerte? Calcule cuánto más fuerte es uno que otro.

(c) Prediga si el siguiente equilibrio favorecerá a los reactivos o a los productos.



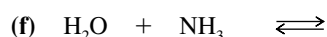
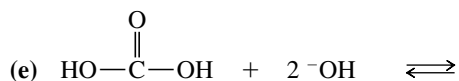
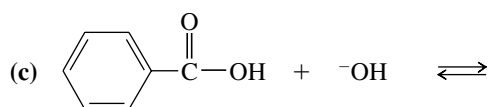
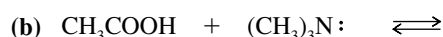
## 1.45

En las siguientes reacciones ácido-base clasifique los reactivos como ácidos de Lewis (electrófilos) o bases de Lewis (nucleófilos). Utilice flechas curvadas para indicar el movimiento de los pares de electrones en las reacciones.



## 1.46

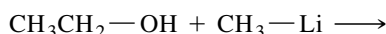
Prediga los productos de las siguientes reacciones ácido-base:



## \*1.47

El metilítio ( $\text{CH}_3\text{Li}$ ) a menudo se usa como base en reacciones orgánicas.

(a) Prediga los productos de la siguiente reacción ácido-base:



(b) ¿Cuál es el ácido conjugado del  $\text{CH}_3\text{Li}$ ? ¿Qué es el  $\text{CH}_3\text{Li}$ ?, ¿una base fuerte o débil?

## \*1.48

En 1984, Edward A. Doisy de la Universidad de Washington extrajo 1 360 kg de ovarios de cerda para aislar unos pocos miligramos de estradiol puro, una potente hormona femenina. Doisy quemó 5.00 mg de esa preciada muestra en oxígeno y encontró que se obtenían 14.54 mg de  $\text{CO}_2$  y 3.97 mg de  $\text{H}_2\text{O}$ .

(a) Determine la fórmula empírica del estradiol.

(b) La masa molecular del estradiol se determinó posteriormente y se encontró que era de 272. Determine la fórmula molecular del estradiol.

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# *Química Orgánica*

*Recopilación*

*José A. - UHNMOSM*



2009

# *Química Orgánica*

## *Recopilación*



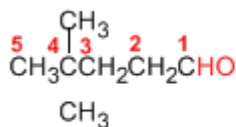
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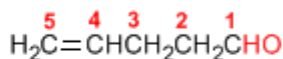
## Nomenclatura de Aldehídos y Cetonas

Los aldehídos se nombran reemplazando la terminación **-ano** del alcano correspondiente por **-al**. No es necesario especificar la posición del grupo aldehído, puesto que ocupa el extremo de la cadena (localizador 1).

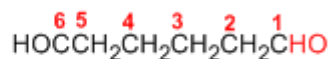
Cuando la cadena contiene dos funciones aldehído se emplea el sufijo **-dial**.



4,4-Dimetilpentanal

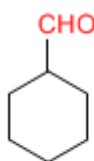


Hex-4-enal

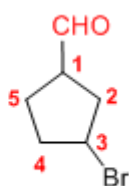


Pentanodial

El grupo **-CHO** unido a un ciclo se llama **-carbaldehído**. La numeración del ciclo se realiza dando localizador 1 al carbono del ciclo que contiene el grupo aldehído.



Ciclohexanocarbaldehído

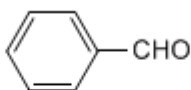


3-Bromociclopentanocarbaldehído

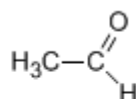
Algunos nombres comunes de aldehídos aceptados por la IUPAC son:



Formaldehído  
(Metanal)

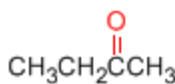


Benzaldehído  
(Bencenocarbaldehído)

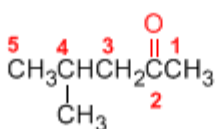


Acetaldehído  
(Etanal)

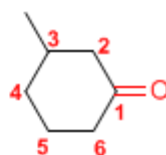
Las cetonas se nombran sustituyendo la terminación **-ano** del alcano con igual longitud de cadena por **-ona**. Se toma como cadena principal la de mayor longitud que contiene el grupo carbonilo y se numera para que éste tome el localizador más bajo.



Butanona

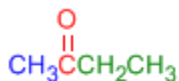


4-Metil-2-pentanona

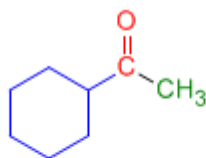


3-Metilciclohexanona

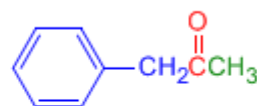
Existe un segundo tipo de nomenclatura para las cetonas, que consiste en nombrar las cadenas como sustituyentes, ordenándolas alfabéticamente y terminando el nombre con la palabra **cetona**.



Etil metil cetona



Ciclohexil metil cetona



Fenil metil cetona

[Siguiete >](#)

[\[Volver\]](#)

## Charles Friedel (1832 - 1899)



**Origen:** Químico frances..

**Lugar de nacimiento:** Estrasburgo.

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

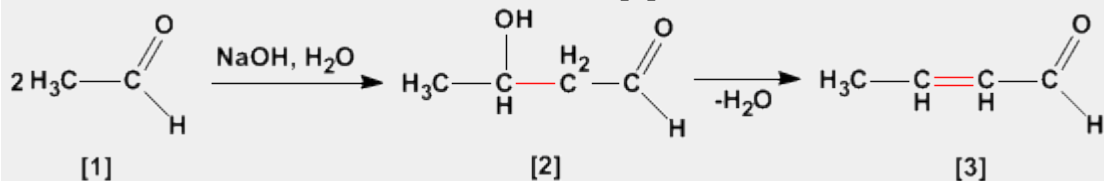
**Docencia:** Profesor en la Universidad de la Sorbona.

**Investigación:** Obtuvo el alcohol propílico. En 1877, Friedel y Crafts describieron por primera vez la reacción del benceno con un haloalcano en presencia de un ácido de Lewis. Esta reacción produce la alquilación del benceno y se conoce como alquilación de Friedl-Crafts.

**Premio Nobel:**

## Aldólica (Condensación)

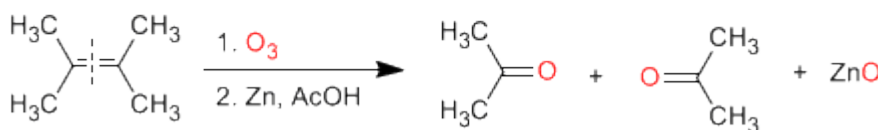
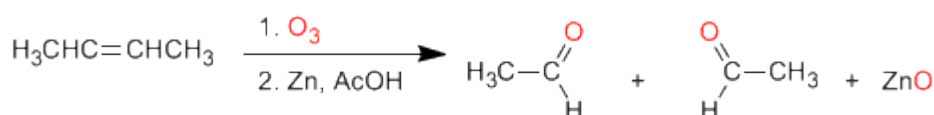
La condensación aldólica es una reacción de aldehídos o cetonas **[1]** que forma 3-hidroxicarbonilos (aldoles) **[2]**. El 3-hidroxialdehído **[2]** bajo condiciones de deshidratación por calentamiento rinde un aldehído alfa,beta-insaturado **[3]**.



## Preparación de aldehídos y cetonas

Los aldehídos y cetonas pueden ser preparados por oxidación de alcoholes, ozonólisis de alquenos, hidratación de alquinos y acilación de Friedel-Crafts como métodos de mayor importancia.

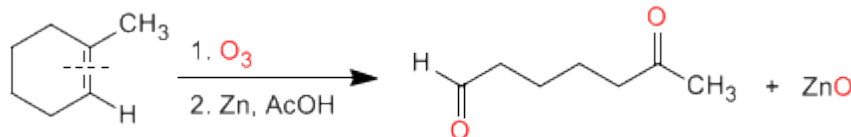
a) **Ozonólisis de alquenos:** Los alquenos rompen con ozono formando aldehídos y/o cetonas. Si el alqueno tiene hidrógenos vinílicos da aldehídos. Si tiene dos cadenas carbonadas forma cetonas.



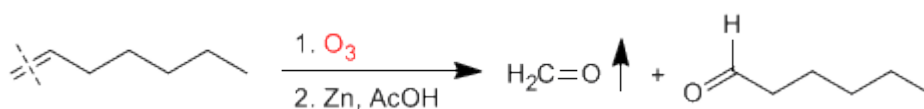
### Ozonólisis

Los alquenos simétricos y terminales permiten la preparación de carbonilos mediante ozonólisis

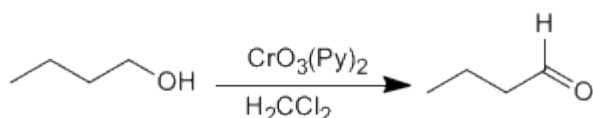
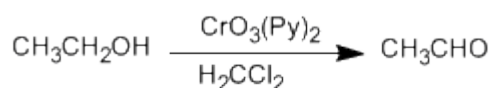
La ozonólisis de alquenos cíclicos produce compuestos dicarbonílicos:



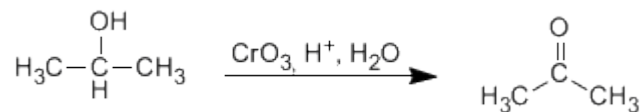
Los alquenos terminales rompen formando metanal, que separa fácilmente de la mezcla por su bajo punto de ebullición.



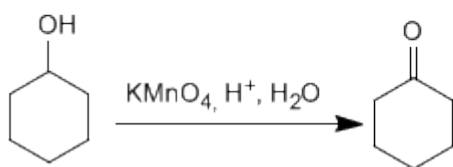
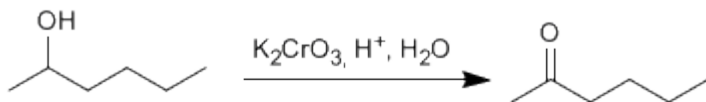
b) **Oxidación de alcoholes:** Los alcoholes primarios y secundarios se oxidan para dar aldehídos y cetonas respectivamente. Deben tomarse precauciones en la oxidación de alcoholes primarios, puesto que sobreoxidan a ácidos carboxílicos en presencia de oxidantes que contengan agua. En estos caso debe trabajarse con reactivos anhidros, como el clorocromato de piridino en diclorometano (PCC), a temperatura ambiente.



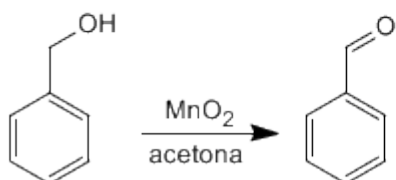
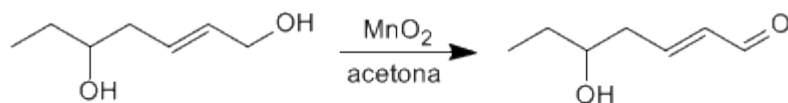
Los alcoholes secundarios dan cetonas por oxidación. Se emplean como oxidantes permanganato, dicromato, trióxido de cromo.



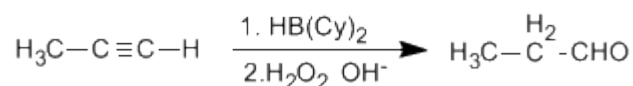
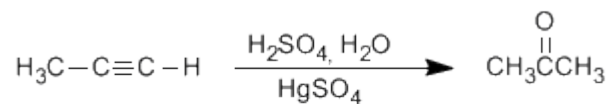
La oxidación supone la pérdida de dos hidrógenos del alcohol. Los alcoholes terciarios no pueden oxidar puesto que carecen de hidrógeno sobre el carbono.



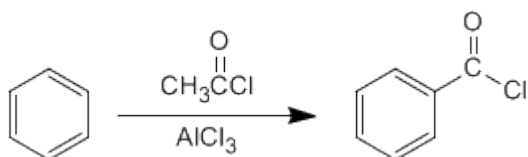
Los alcoholes alílicos y bencílicos se transforman en aldehídos o cetonas por oxidación con dióxido de manganeso en acetona. Esta reacción tiene una elevada selectividad y no oxida alcoholes que no se encuentren en dichas posiciones.



c) **Hidratación de alquinos:** Los alquinos se pueden hidratar Markovnikov, formando cetonas, o bien antiMarkovnikov, para formar aldehídos.



d) **Acilación de Friedel-Crafts:** La introducción de grupos acilo en el benceno permite la preparación de cetonas con cadenas aromáticas.



### Otto Paul Hermann Diels (1876 - 1954)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

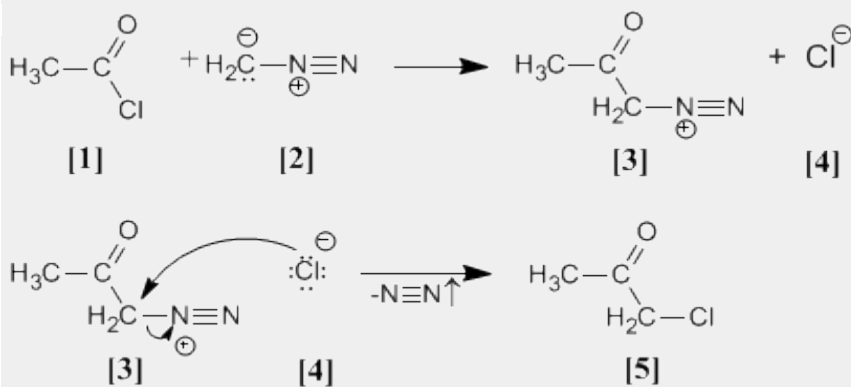
**Docencia:** profesor y jefe del departamento de química en la Universidad de Berlín. En 1916, tomó el puesto de profesor de Química en la Universidad de Kiel, cargo que no dejó hasta su jubilación en 1945.

**Investigación:** En 1906 descubrió el anhídrido malónico. Investigó en reacciones de deshidrogenación con selenio. Síntesis de  $\alpha$ -dicetonas. Pero su trabajo más importante es la reacción de Diels - Alder.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Kurt Alder

### Arndt Eistert (Síntesis)

Cloruro de acetilo [1] se trata con diazometano [2] rindiendo la sal de diazonio [3]. El cloruro [4] producido reacciona con la sal de diazonio para dar la  $\alpha$ -clorocetona [5].

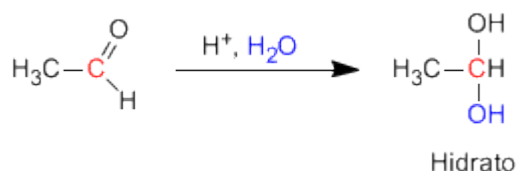


#### Síntesis de Arndt Eistert

Esta reacción permite transformar haluros de alcanoilo en cetonas halogenadas en su posición alfa.

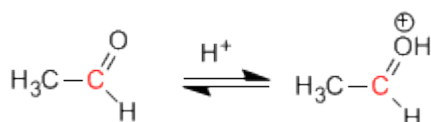
## Formación de Hidratos

Los aldehídos y cetonas reaccionan en medio ácido acuoso para formar hidratos. El mecanismo consta de tres etapas. La primera y más rápida consiste en la protonación del oxígeno carbonílico. Esta protonación produce un aumento de la polaridad sobre el carbono y favorece el ataque del nucleófilo. En la segunda etapa el agua ataca al carbono carbonilo, es la etapa lenta del mecanismo. En la tercera etapa se produce la desprotonación del oxígeno formándose el hidrato final.

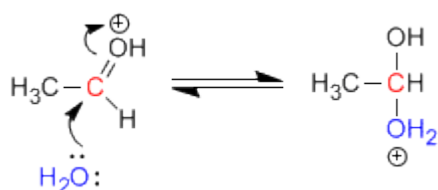


### Mecanismo de la reacción

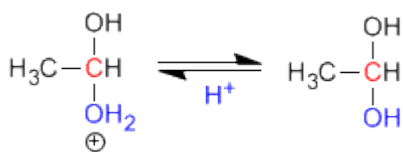
Etapa 1. Protonación del oxígeno carbonílico.



Etapa 2. Ataque nucleófilo del agua al carbonilo protonado.



Etapa 3. Desprotonación del hidrato





**Origen:** Químico estadounidense.

**Lugar de nacimiento:** Budapest

**Formación:** Se doctoró en la Universidad de Budapest en 1949

**Docencia:** Trabajó en el departamento de química orgánica de la Academia de Ciencias de Hungría y posteriormente en la Universidad de Cleveland.

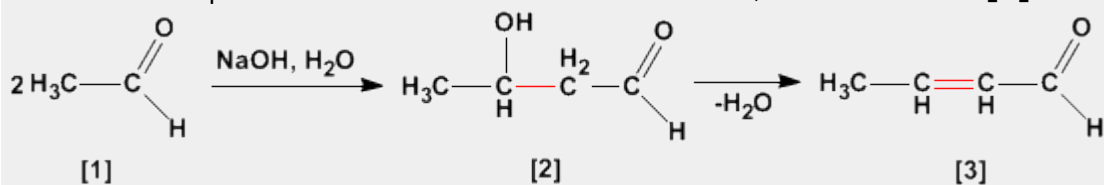
**Industria:** Trabajó en los laboratorios de la Dow Chemical de Ontario

**Investigación:** Olah consiguió preparar carbocationes estables utilizando componentes extremadamente ácidos.

**Premio Nobel:** En 1994 obtuvo el premio Nobel de Química por sus investigaciones sobre los carbocationes

### Aldólica (Condensación)

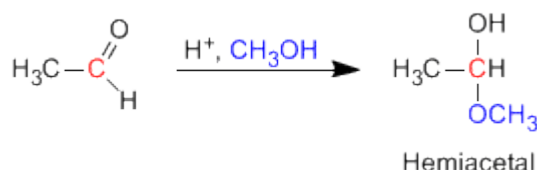
La condensación aldólica es una reacción de aldehídos o cetonas **[1]** que forma 3-hidroxicarbonilos (aldoles) **[2]**. El 3-hidroxialdehído **[2]** bajo condiciones de deshidratación por calentamiento rinde un aldehído alfa,beta-insaturado **[3]**.





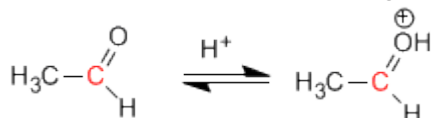
## Formación de Hemiacetales

Los hemiacetales se forman por reacción de un equivalente de alcohol con el grupo carbonilo de un aldehído o cetona. Esta reacción se cataliza con ácido y es equivalente a la formación de hidratos.

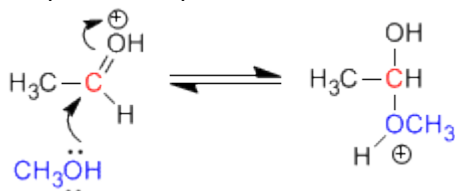


### Mecanismo de la reacción:

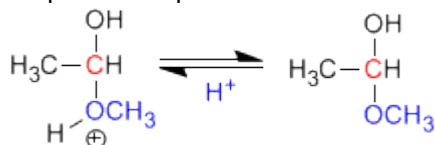
Eta 1. Protonación del oxígeno carbonílico.



Eta 2. Ataque nucleófilo del metanol al carbonilo protonado.



Eta 3. Desprotonación del hemiacetal



### Otto Paul Hermann Diels (1876 - 1954)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

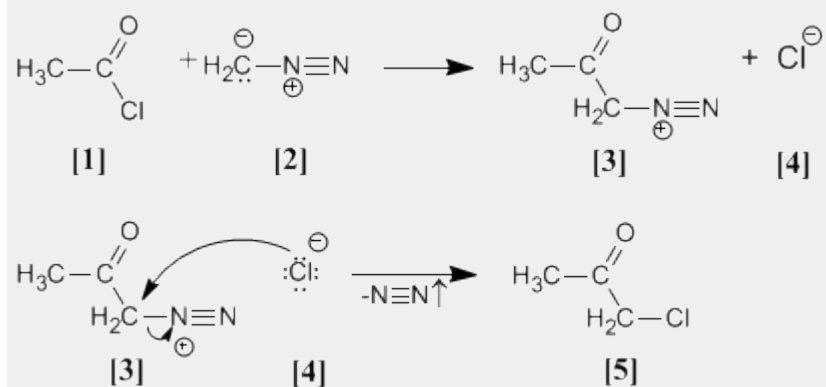
**Docencia:** profesor y jefe del departamento de química en la Universidad de Berlín. En 1916, tomó el puesto de profesor de Química en la Universidad de Kiel, cargo que no dejó hasta su jubilación en 1945.

**Investigación:** En 1906 descubrió el anhídrido malónico. Investigó en reacciones de deshidrogenación con selenio. Síntesis de  $\alpha$ -dicetonas. Pero su trabajo más importante es la reacción de Diels - Alder.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Kurt Alder

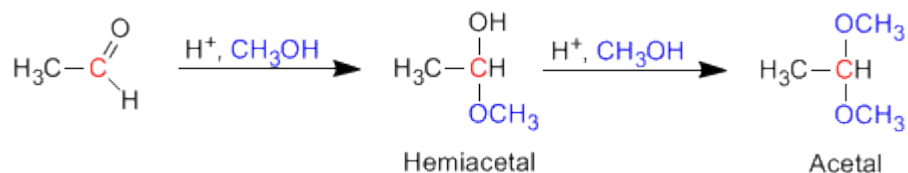
### Arndt Eistert (Síntesis)

Cloruro de acetilo **[1]** se trata con diazometano **[2]** rindiendo la sal de diazonio **[3]**. El cloruro **[4]** producido reacciona con la sal de diazonio para dar la  $\alpha$ -clorocetona **[5]**.



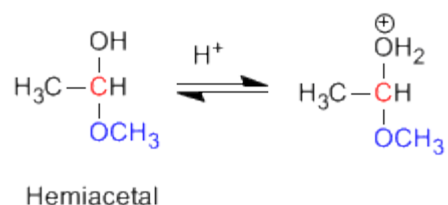
## Formación de Acetales

Los aldehídos y cetonas reaccionan con alcoholes bajo condiciones de catálisis ácida, formando en una primera etapa hemiacetales, que posteriormente evolucionan por reacción con un segundo equivalente de alcohol a acetales.

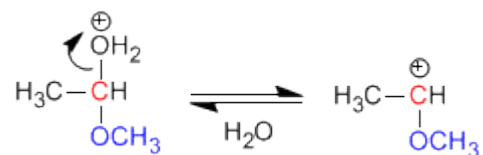


### Mecanismo para la formación de acetales

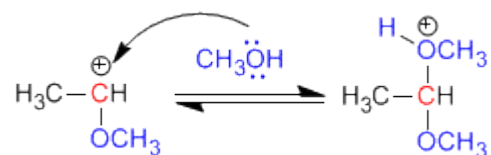
Etapa 1. Protonación del grupo hidroxilo



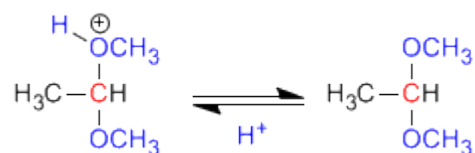
Etapa 2. Pérdida de agua.



Etapa 3. Ataque del alcohol al carbocatión



Etapa 4. Desprotonación del acetal



### Otto Paul Hermann Diels (1876 - 1954)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

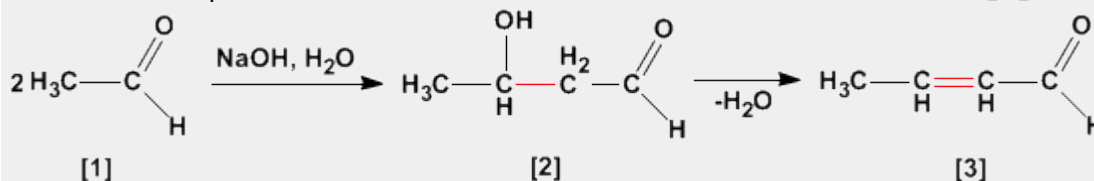
**Docencia:** profesor y jefe del departamento de química en la Universidad de Berlín. En 1916, tomó el puesto de profesor de Química en la Universidad de Kiel, cargo que no dejó hasta su jubilación en 1945.

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**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Kurt Alder

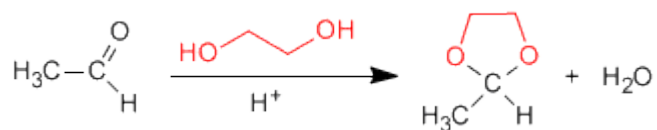
### Aldólica (Condensación)

La condensación aldólica es una reacción de aldehídos o cetonas **[1]** que forma 3-hidroxicarbonilos (aldoles) **[2]**. El 3-hidroxialdehído **[2]** bajo condiciones de deshidratación por calentamiento rinde un aldehído alfa,beta-insaturado **[3]**.



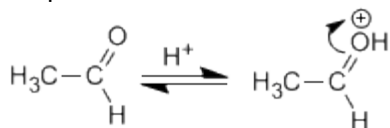
## Formación de acetales cíclicos

Los 1,2- y 1,3-dioles reaccionan con aldehídos y cetonas formando acetales cíclicos. Los equilibrios se desplazan hacia el producto final eliminando el agua formada por destilación azeotrópica con benceno o tolueno.

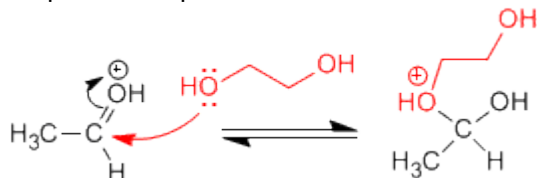


### Mecanismo para la formación de acetales cíclicos:

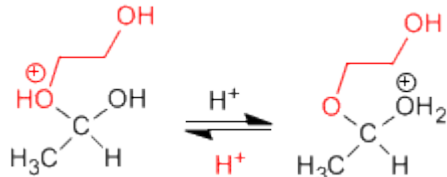
Etapa 1. Protonación del carbonilo



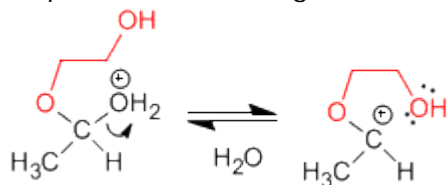
Etapa 2. Ataque nucleófilo del diol al carbonilo.



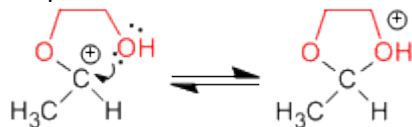
Etapa 3. Equilibrio ácido base entre el éter y el alcohol



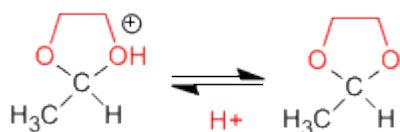
Etapa 4. Pérdida de agua



Etapa 5. Ciclación



Etapa 6. Desprotonación del acetal cíclico



### Kurt Alder (1902 - 1958)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió en la Universidad de Kiel. Bajo la supervisión del químico alemán Otto Diels, su jefe e instructor en Kiel.

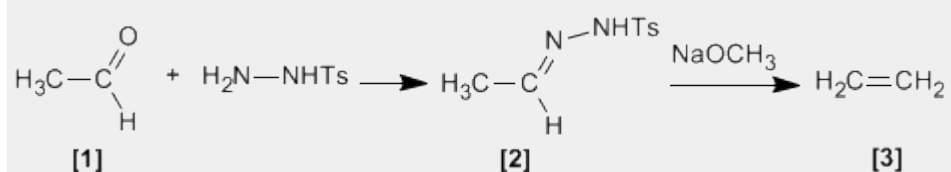
**Docencia:** Alder ejerció como profesor de química en las universidades de Kiel y Colonia.

**Investigación:** Alder se especializó en la síntesis diénica (conocida más tarde como la reacción Diels - Alder) que consiste fundamentalmente en el análisis y formación de compuestos orgánicos complejos. Ya en 1928 ambos fueron coautores de un ensayo sobre este proceso.

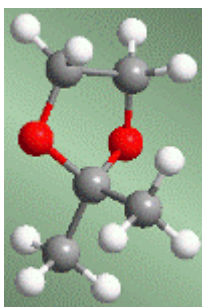
**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Diels

### Bamford Stevens (Reacción)

Tosilhidrazonas [2] de aldehídos o cetonas alifáticos [1] reaccionan con bases fuertes para dar alquenos [3].

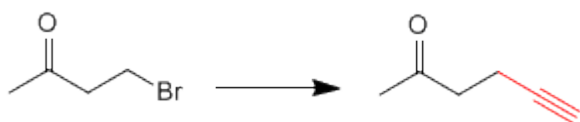


## Acetales como grupos protectores

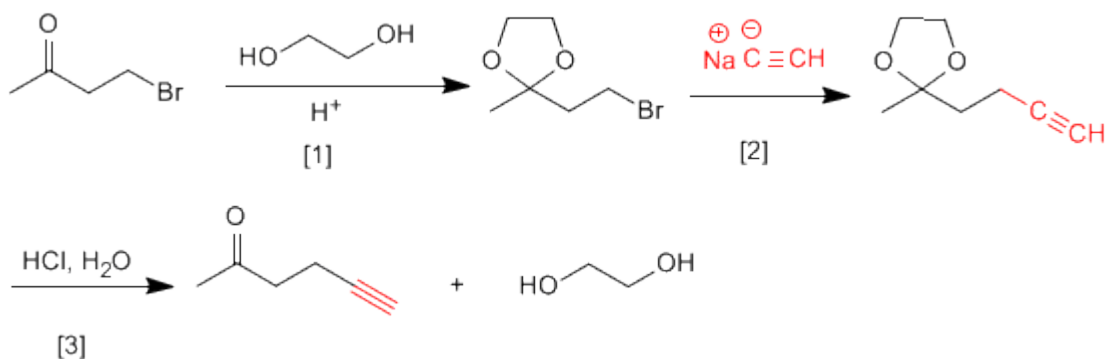


Los acetales pueden emplearse, por su estabilidad, como grupos protectores del carbonilo. El acetal es un éter, muy estable en medios básicos, aunque rompe en presencia de medios ácidos. En muchos procesos de síntesis el grupo carbonilo es incompatible con el reactivo utilizado. En estos casos debe protegerse para evitar que reaccione. La inestabilidad del acetal en medio ácido puede emplearse para desproteger el carbonilo.

Veamos algunos ejemplos:



Esta transformación requiere una sustitución, empleando como nucleófilo un acetiluro de sodio. El nucleófilo puede atacar también al grupo carbonilo, para evitarlo vamos a protegerlo.

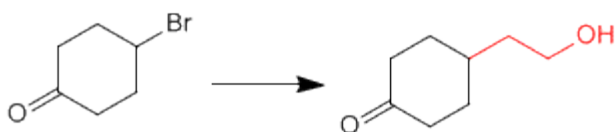


[1] Protección de la cetona.

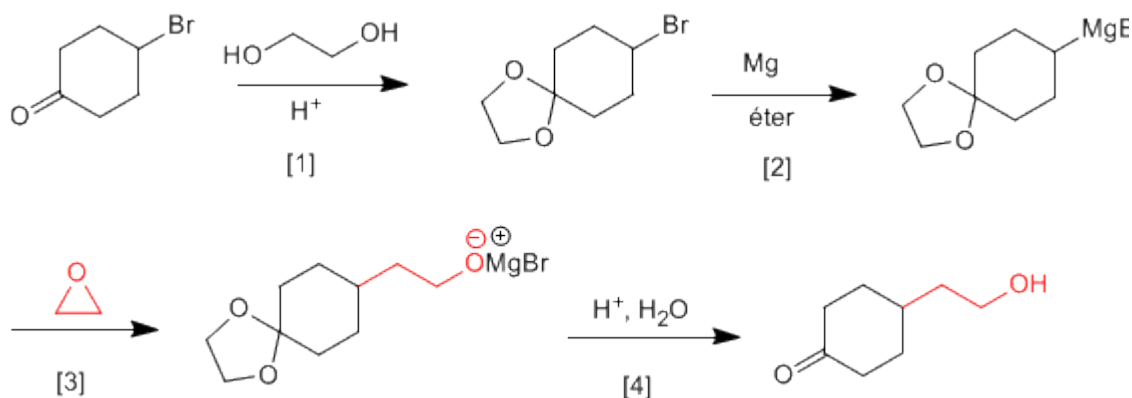
[2] Ataque del acetiluro al carbono del bromo.

[3] Desprotección del carbonilo

Veamos un segundo ejemplo:



Es necesario proteger la cetona antes de formar el organometálico para evitar la dimerización del compuesto.



- [1] Protección de la cetona.  
 [2] Formación del magnesiano.  
 [3] Apertura del oxaciclopropano.  
 [4] Desprotección y protonación del alcóxido.

### Otto Paul Hermann Diels (1876 - 1954)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

**Docencia:** profesor y jefe del departamento de química en la Universidad de Berlín. En 1916, tomó el puesto de profesor de Química en la Universidad de Kiel, cargo que no dejó hasta su jubilación en 1945.

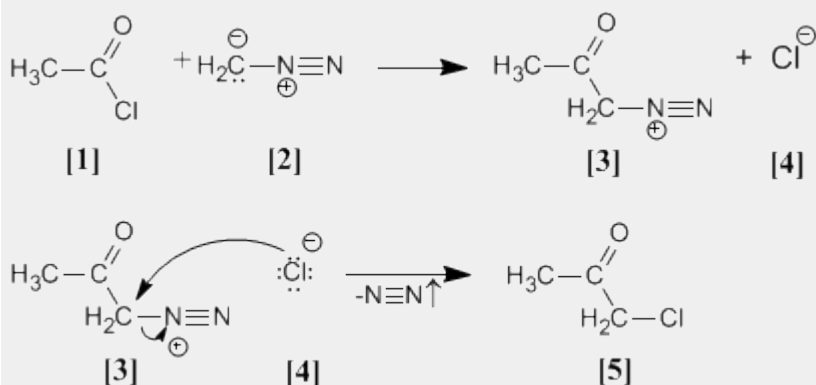
**Investigación:** En 1906 descubrió el anhídrido malónico.

Investigó en reacciones de deshidrogenación con selenio. Síntesis de  $\alpha$ -dicetonas. Pero su trabajo más importante es la reacción de Diels - Alder.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Kurt Alder

### Arndt Eistert (Síntesis)

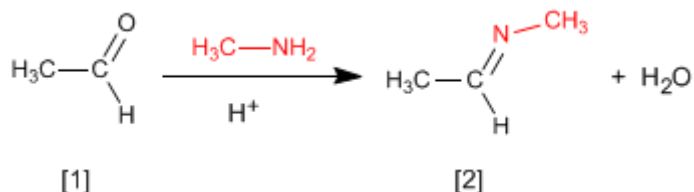
Cloruro de acetilo **[1]** se trata con diazometano **[2]** rindiendo la sal de diazonio **[3]**. El cloruro **[4]** producido reacciona con la sal de diazonio para dar la  $\alpha$ -clorocetona **[5]**.





## Formación de Iminas

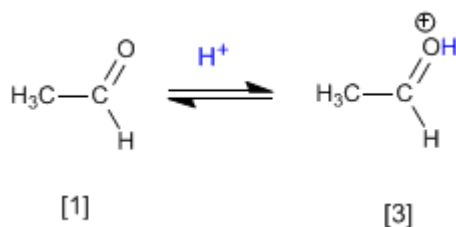
La reacción de aldehídos o cetonas **[1]** con aminas primarias genera iminas **[2]**. La reacción se favorece en un medio ligeramente ácido (pH=4.5).



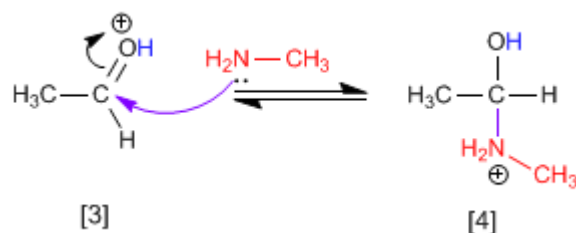
El control del pH es fundamental, puesto que se requiere la protonación del oxígeno del carbonilo para favorecer el ataque nucleófilo.

### Mecanismo:

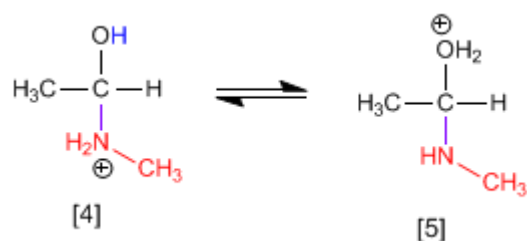
**Etapla 1.** Protonación del grupo carbonilo que aumenta la polaridad positiva sobre el carbono y favorece el ataque nucleófilo.



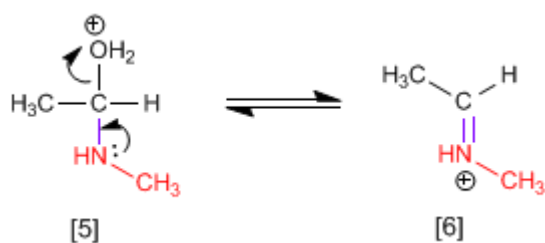
**Etapla 2.** Ataque nucleófilo de la amina primaria al carbono carbonilo.



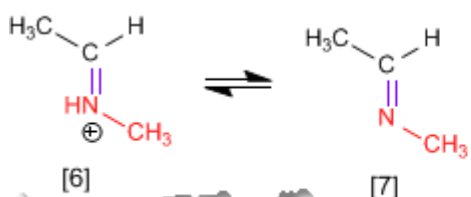
**Etapla 3.** Protonación del grupo hidroxilo para transformarlo en buen grupo saliente.



**Etapla 4.** Pérdida de agua y formación de la imina protonada.



### Etapa 5. Desprotonación del catión.



### George A. Olah (1927 - )



**Origen:** Químico estadounidense.

**Lugar de nacimiento:** Budapest

**Formación:** Se doctoró en la Universidad de Budapest en 1949

**Docencia:** Trabajó en el departamento de química orgánica de la Academia de Ciencias de Hungría y posteriormente en la

Universidad de Cleveland.

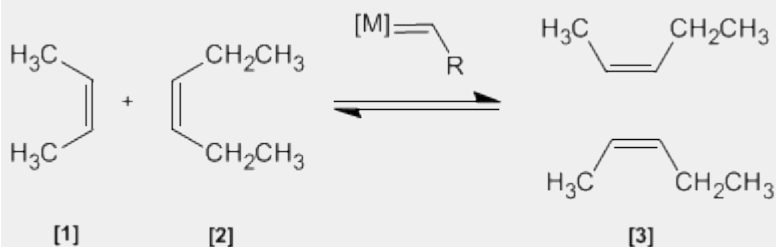
**Industria:** Trabajó en los laboratorios de la Dow Chemical de Ontario

**Investigación:** Olah consiguió preparar carbocationes estables utilizando componentes extremadamente ácidos.

**Premio Nobel:** En 1994 obtuvo el premio Nobel de Química por sus investigaciones sobre los carbocationes

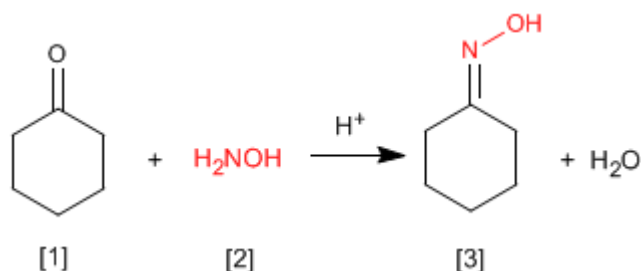
### Metátesis de Alquenos

En esta reacción dos alquenos **[1]** y **[2]** son tratados con un metal de transición que actúa como catalizador, dando una mezcla de alquenos **[3]** (incluyendo isómeros Z/E). Este productos se obtiene por intercambio de grupos alquilideno.

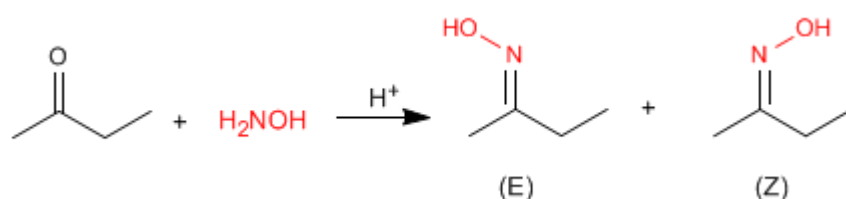


## Formación de Oximas

Las oximas [3] se obtienen por reacción de aldehídos o cetonas [1] e hidroxilamina [2] en un medio débilmente ácido. El mecanismo es análogo al de formación de iminas.



Las oximas de aldehídos y cetona asimétricas presentan isomería Z/E dependiendo de la posición del hidroxilo.



Las iminas e hidrazonas (que comentaremos a continuación) también presentan esta característica.

### George A. Olah (1927 - )



**Origen:** Químico estadounidense.

**Lugar de nacimiento:** Budapest

**Formación:** Se doctoró en la Universidad de Budapest en 1949

**Docencia:** Trabajó en el departamento de química orgánica de la Academia de Ciencias de Hungría y posteriormente en la Universidad de Cleveland.

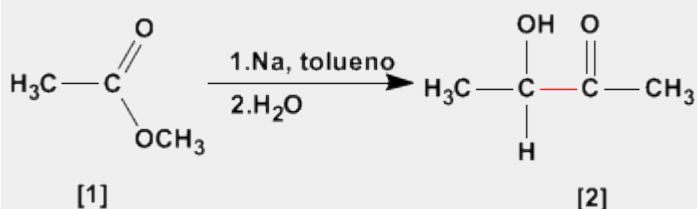
**Industria:** Trabajó en los laboratorios de la Dow Chemical de Ontario

**Investigación:** Olah consiguió preparar carbocationes estables utilizando componentes extremadamente ácidos.

**Premio Nobel:** En 1994 obtuvo el premio Nobel de Química por sus investigaciones sobre los carbocationes

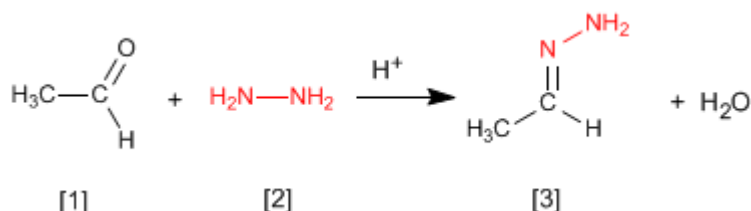
## Aciloinica (Condensación)

La condensación aciloinica transforma ésteres [1] en alfa-hidroxicetonas [2]. Esta reacción se realiza con sodio metal en disolvente inerte.

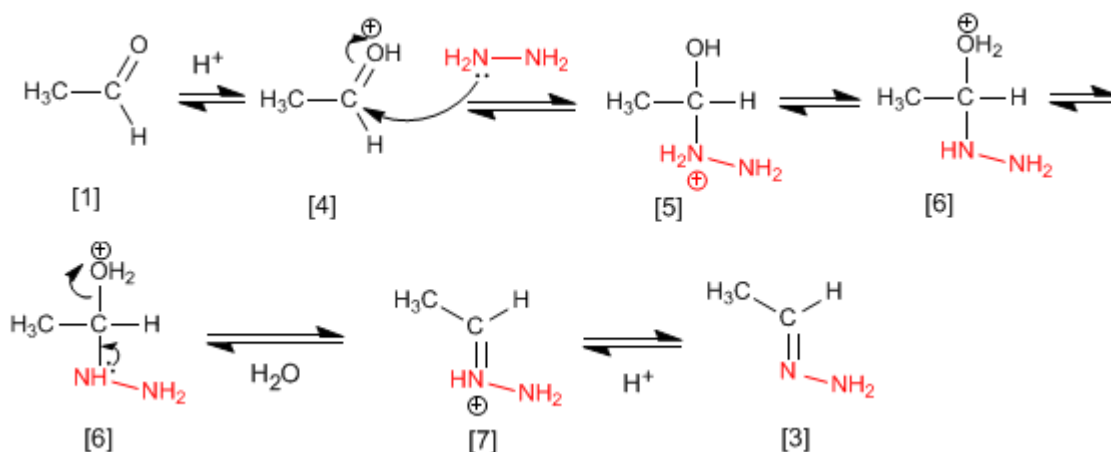


## Formación de Hidrazonas

Las hidrazonas [3] se obtienen por reacción de aldehídos o cetonas [1] con hidrazina [2]. Igual que en el caso de las iminas y oximas requiere pH=4.



Aunque el mecanismo es análogo al de formación de iminas, comentaremos de nuevo los pasos.



El etanal [1] se protona formando su ácido conjugado [4]. La importante polaridad del carbono carbonilo de [4] favorece el ataque de la hidrazina [2] para formando el intermedio [5]. El compuesto [5] intercambia un protón entre el nitrógeno y el oxígeno, transformando el grupo hidroxilo en agua (buen grupo saliente). El intermedio [6] pierde una molécula de agua transformándose en [7], cuya desprotonación da la hidrazona final [3].

### Kurt Alder (1902 - 1958)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió en la Universidad de Kiel. Bajo la supervisión del químico alemán Otto Diels, su jefe e instructor en Kiel.

**Docencia:** Alder ejerció como profesor de química en las universidades de Kiel y Colonia.

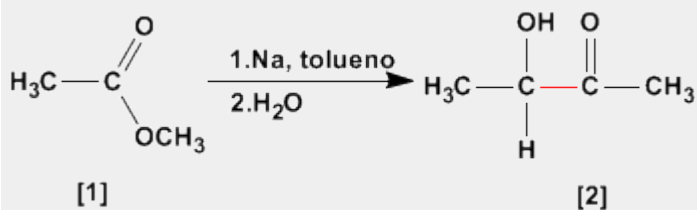
**Investigación:** Alder se especializó en la síntesis diénica (conocida más tarde como la reacción Diels - Alder) que consiste fundamentalmente en el análisis y formación de compuestos orgánicos complejos.

Ya en 1928 ambos fueron coautores de un ensayo sobre este proceso.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Diels

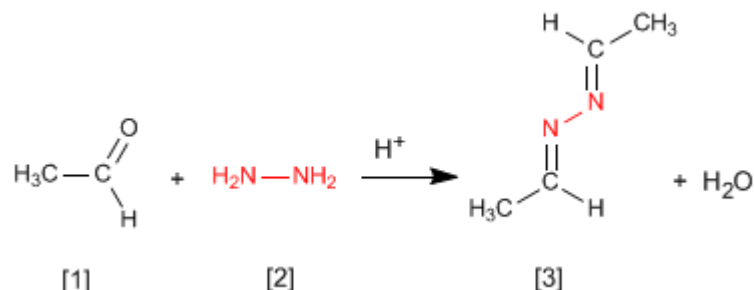
### Aciloínica (Condensación)

La condensación aciloínica transforma esteres [1] en alfa-hidroxicetonas [2]. Esta reacción se realiza con sodio metal en disolvente inerte.



## Formación de Azinas

La hidrazina [2] reacciona con dos moléculas de aldehído [1] para formar azinas [3].



El mecanismo es análogo al de formación de iminas, oximas e hidrazonas.

### George A. Olah (1927 - )



**Origen:** Químico estadounidense.

**Lugar de nacimiento:** Budapest

**Formación:** Se doctoró en la Universidad de Budapest en 1949

**Docencia:** Trabajó en el departamento de química orgánica de la Academia de Ciencias de Hungría y posteriormente en la

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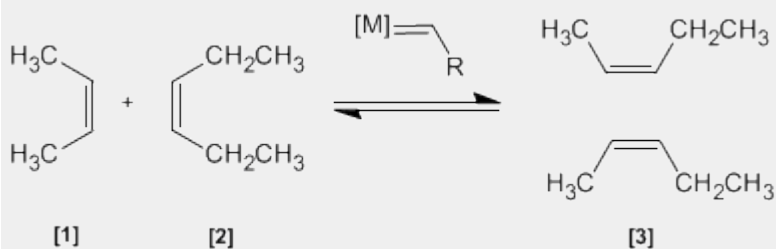
**Industria:** Trabajó en los laboratorios de la Dow Chemical de Ontario

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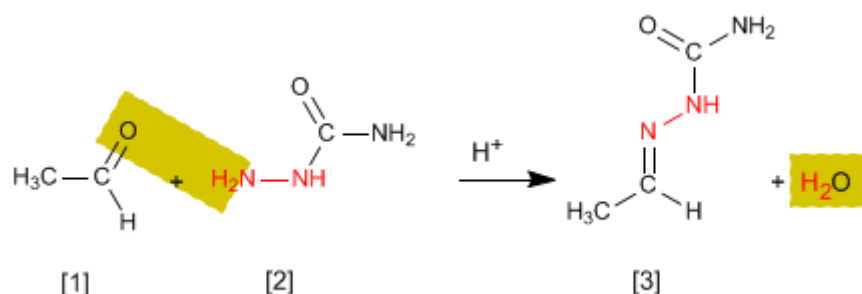
## Metátesis de Alquenos

En esta reacción dos alquenos [1] y [2] son tratados con un metal de transición que actúa como catalizador, dando una mezcla de alquenos [3] (incluyendo isómeros Z/E). Este producto se obtiene por intercambio de grupos alquilideno.



## Formación de Semicarbazonas

Las semicarbazonas [3] se obtienen por reacción de aldehídos o cetonas [1] con semicarbazida [2]. Veamos un ejemplo:



El mecanismo es análogo al de formación de iminas, oximas e hidrazonas.

### Charles Friedel (1832 - 1899)



**Origen:** Químico frances..

**Lugar de nacimiento:** Estrasburgo.

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

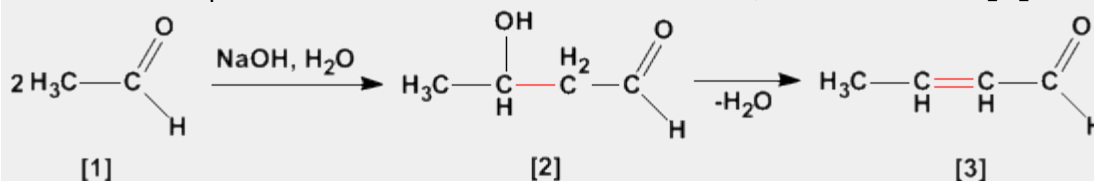
**Docencia:** Profesor en la Universidad de la Sorbona.

**Investigación:** Obtuvo el alcohol propílico. En 1877, Friedel y Crafts describieron por primera vez la reacción del benceno con un haloalcano en presencia de un ácido de Lewis. Esta reacción produce la alquilación del benceno y se conoce como alquilación de Friedl-Crafts.

**Premio Nobel:**

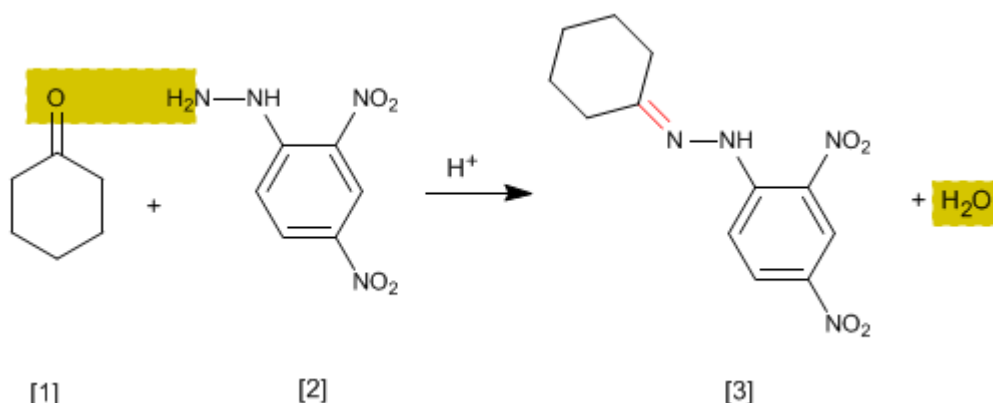
### Aldólica (Condensación)

La condensación aldólica es una reacción de aldehídos o cetonas [1] que forma 3-hidroxicarbonilos (aldoles) [2]. El 3-hidroxialdehído [2] bajo condiciones de deshidratación por calentamiento rinde un aldehído alfa,beta-insaturado [3].



## Ensayo de la 2,4-Dinitrofenilhidrazina

Se trata de un ensayo analítico específico de aldehídos y cetonas. Los carbonilos **[1]** reaccionan con 2,4-Dinitrofenilhidrazina **[2]** formando fenilhidrazonas **[3]** que precipitan de color amarillo. La aparición de precipitado es un indicador de la presencia de carbonilos en el medio.



El mecanismo de la reacción es análogo al de formación de iminas.

### Kurt Alder (1902 - 1958)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió en la Universidad de Kiel. Bajo la supervisión del químico alemán Otto Diels, su jefe e instructor en Kiel.

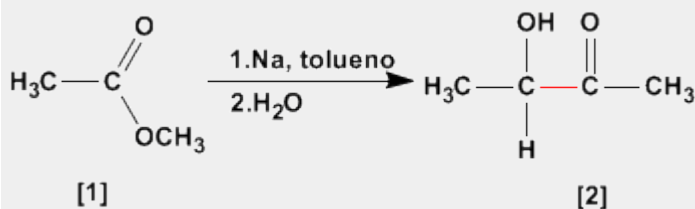
**Docencia:** Alder ejerció como profesor de química en las universidades de Kiel y Colonia.

**Investigación:** Alder se especializó en la síntesis diénica (conocida más tarde como la reacción Diels - Alder) que consiste fundamentalmente en el análisis y formación de compuestos orgánicos complejos. Ya en 1928 ambos fueron coautores de un ensayo sobre este proceso.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Diels

### Aciloinica (Condensación)

La condensación aciloinica transforma esteres **[1]** en alfa-hidroxicetonas **[2]**. Esta reacción se realiza con sodio metal en disolvente inerte.





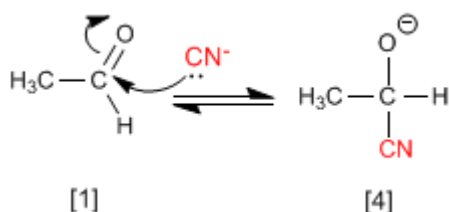
## Formación de Cianhidrinas

Las cianhidrinas **[3]** se forman por reacción de aldehídos o cetonas **[1]** con ácido cianhídrico **[2]** y son compuestos que contienen un grupo ciano y un hidroxilo sobre el mismo carbono.

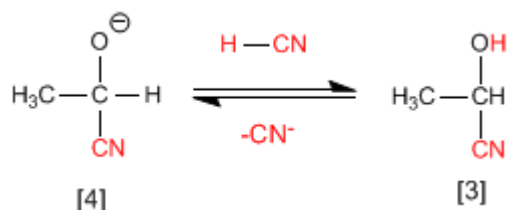


El mecanismo de la reacción transcurre en dos etapas:

**Etapla 1.** Los iones cianuro actúan como nucleófilos atacando al carbono carbonilo. El ácido cianhídrico es demasiado débil para generar cantidades importantes de cianuro, por ello, se añade cianuro de sodio o potasio al medio, garantizando la cantidad suficiente de cianuro para que la reacción transcurra en buen rendimiento.



**Etapla 2.** En este paso el ión alcóxido **[4]** se protona arrancando hidrógenos al ácido cianhídrico. En esta etapa se regeneran los iones cianuro.



### Kurt Alder (1902 - 1958)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió en la Universidad de Kiel. Bajo la supervisión del químico alemán Otto Diels, su jefe e instructor en Kiel.

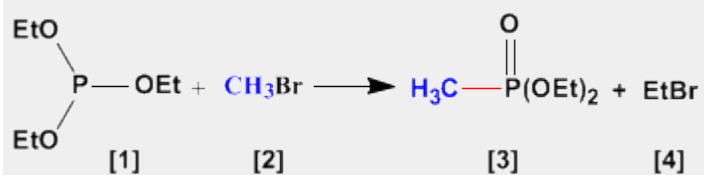
**Docencia:** Alder ejerció como profesor de química en las universidades de Kiel y Colonia.

**Investigación:** Alder se especializó en la síntesis diénica (conocida más tarde como la reacción Diels - Alder) que consiste fundamentalmente en el análisis y formación de compuestos orgánicos complejos. Ya en 1928 ambos fueron coautores de un ensayo sobre este proceso.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Diels

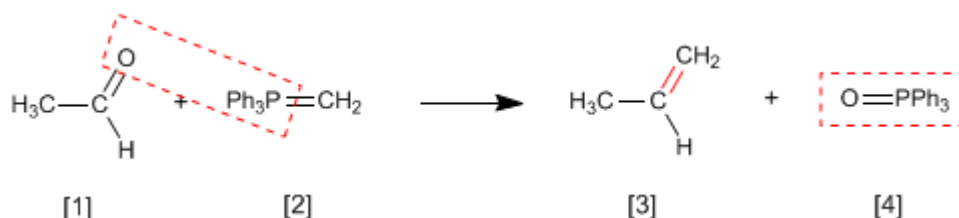
### Arbuzov (Reacción)

La reacción de Arbuzov se emplea en la síntesis de fosfonatos **[3]** a partir de fosfitos **[1]**. Los fosfonatos obtenidos en la síntesis de Arbuzov se emplean como materiales de partida en la síntesis de Horner-Wittig.



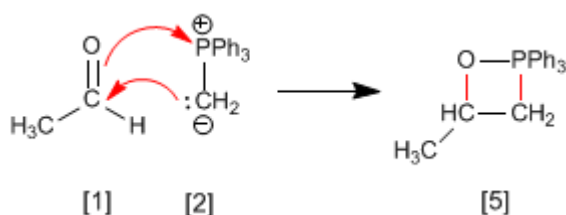
## Reacción de Wittig

La reacción de Wittig emplea iluros de fósforo [2] para transformar aldehídos y cetonas [1] en alquenos [3]. Como subproducto se obtiene el óxido de trifenilfosfina [4].

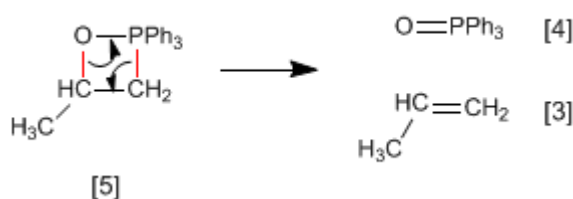


En el mecanismo de la reacción el iluro y el carbonilo se combinan para formar un oxafosfetano que rompe dejando libre el alqueno final.

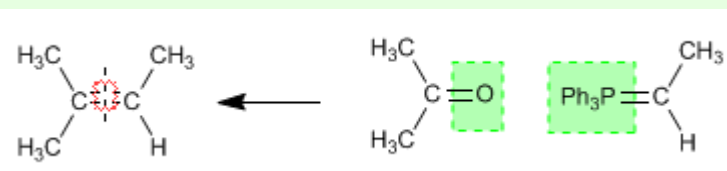
**Etapas 1.** El etanal y el iluro se combinan formando el fosfetano.



**Etapas 2.** El fosfetano rompe formando el alqueno y óxido de trifenilfosfina.



Ejemplo - Obtener mediante Wittig el 2-Metilbut-2-eno



Se rompe el alqueno por el doble enlace y a cada carbono se le agrega el grupo encerrado en verde.

Los **iluros de fósforo** se preparan mediante reacción de haloalcanos y trifenilfosfina, seguido de desprotonación del carbono con base fuerte (organometálicos de litio).



### Charles Friedel (1832 - 1899)



**Origen:** Químico frances..

**Lugar de nacimiento:** Estrasburgo.

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

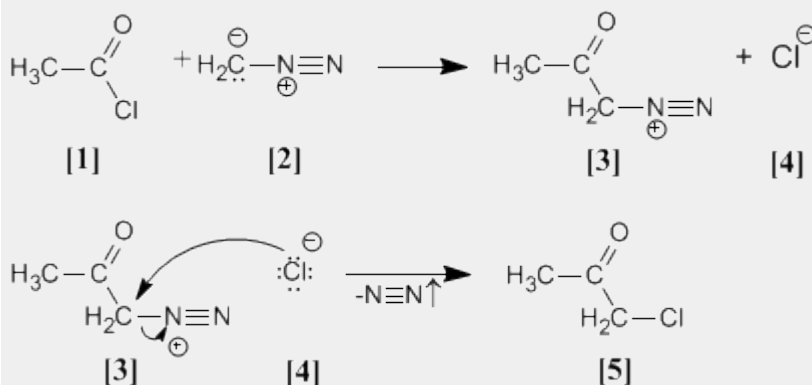
**Docencia:** Profesor en la Universidad de la Sorbona.

**Investigación:** Obtuvo el alcohol propílico. En 1877, Friedel y Crafts describieron por primera vez la reacción del benceno con un haloalcano en presencia de un ácido de Lewis. Esta reacción produce la alquilación del benceno y se conoce como alquilación de Friedl-Crafts.

**Premio Nobel:**

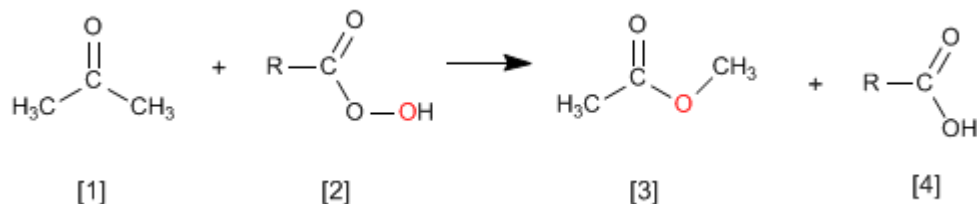
### Arndt Eistert (Síntesis)

Cloruro de acetilo **[1]** se trata con diazometano **[2]** rindiendo la sal de diazonio **[3]**. El cloruro **[4]** producido reacciona con la sal de diazonio para dar la α-clorocetona **[5]**.

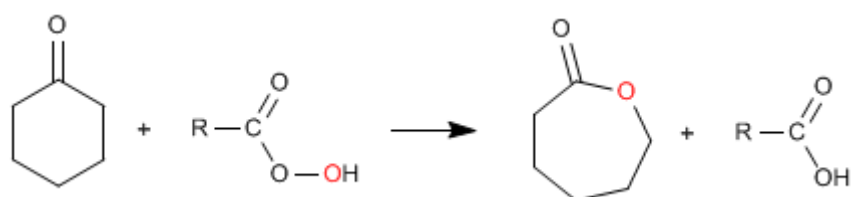


## Oxidación de Baeyer Villiger

La reacción de cetonas **[1]** con perácidos **[2]** produce ésteres **[3]**. El oxígeno del perácido se inserta entre el carbono carbonilo y el carbono alfa de la cetona. Esta reacción fue descrita por Adolf von Baeyer y Victor Villiger in 1899.

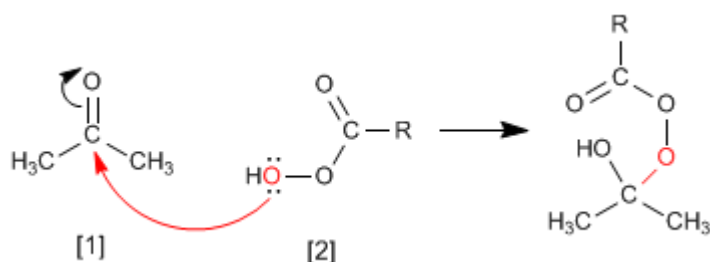


A partir de cetonas cíclicas se obtienen ésteres cíclicos (lactonas)

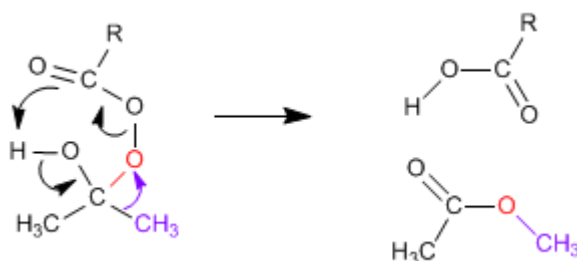


El mecanismo de Baeyer Villiger comienza con el ataque nucleófilo del perácido sobre el carbonilo, seguido de la migración del sustituyente desde el grupo carbonilo al oxígeno del perácido.

**Etapas 1.** Adición del perácido al carbonilo

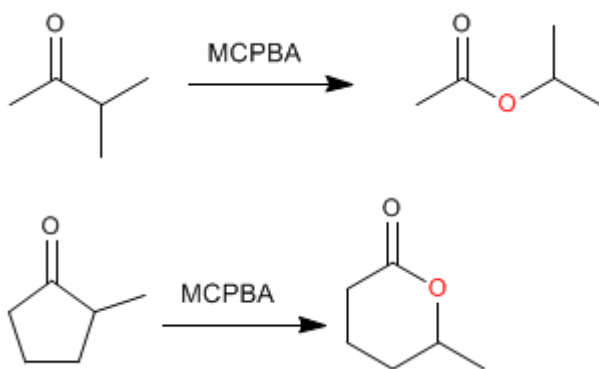


**Etapas 2.** Migración del sustituyente desde carbono carbonilo hacia el oxígeno (rojo)

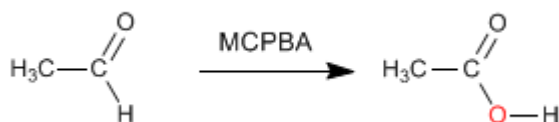


Cuando la cetona tiene dos sustituyentes diferentes migra mejor el más sustituido. Existe un orden de migración que nos ayuda a decidir que sustituyente pasa a unirse al oxígeno del perácido.

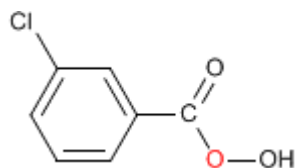
Orden de migración: H > carbono terciario > ciclohexilo > carbono secundario » fenilo > carbono primario > metilo



Como puede observarse en el orden de migración, el grupo que mejor migra, por su pequeño tamaño, es el hidrógeno, por ello, al tratar aldehídos con perácidos se produce la migración del hidrógeno formándose ácidos carboxílicos.



El **MCPBA** (Ácido meta-cloroperoxibenzoico) es un perácido ampliamente utilizado en la epoxidación de alquenos y también en Baeyer-Villger. La fórmula del MCPBA se muestra a continuación.



#### Charles Friedel (1832 - 1899)



**Origen:** Químico frances..

**Lugar de nacimiento:** Estrasburgo.

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

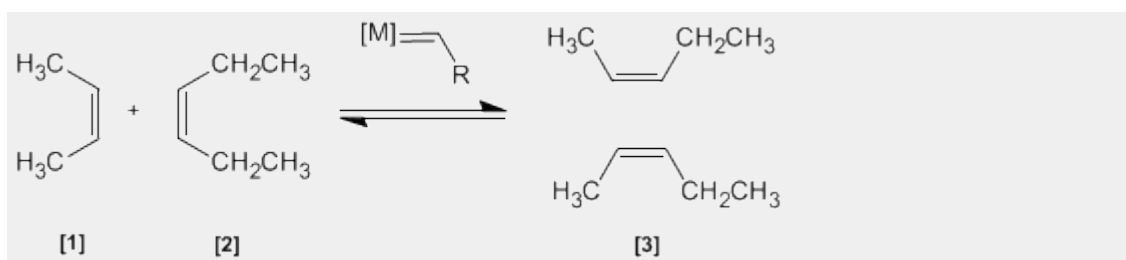
**Docencia:** Profesor en la Universidad de la Sorbona.

**Investigación:** Obtuvo el alcohol propílico. En 1877, Friedel y Crafts describieron por primera vez la reacción del benceno con un haloalcano en presencia de un ácido de Lewis. Esta reacción produce la alquilación del benceno y se conoce como alquilación de Friedl-Crafts.

**Premio Nobel:**

#### Metátesis de Alquenos

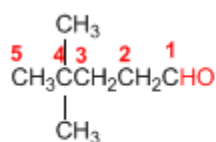
En esta reacción dos alquenos **[1]** y **[2]** son tratados con un metal de transición que actúa como catalizador, dando una mezcla de alquenos **[3]** (incluyendo isómeros Z/E). Este productos se obtiene por intercambio de grupos alquilideno.



## Nomenclatura de Aldehídos y Cetonas - Reglas IUPAC

**Regla 1.** Los aldehídos se nombran reemplazando la terminación **-ano** del alcano correspondiente por **-al**. No es necesario especificar la posición del grupo aldehído, puesto que ocupa el extremo de la cadena (localizador 1).

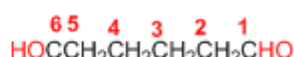
Cuando la cadena contiene dos funciones aldehído se emplea el sufijo **-dial**.



4,4-Dimetilpentanal

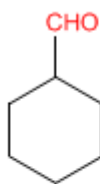


Hex-4-enal

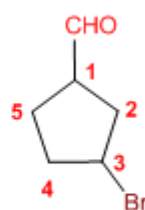


Hexanodial

**Regla 2.** El grupo **-CHO** se denomina **-carbaldehído**. Este tipo de nomenclatura es muy útil cuando el grupo aldehído va unido a un ciclo. La numeración del ciclo se realiza dando localizador 1 al carbono del ciclo que contiene el grupo aldehído.

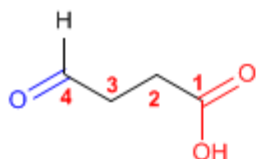


Ciclohexanocarbaldehído

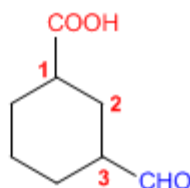


3-Bromociclopentanocarbaldehído

**Regla 3.** Cuando en la molécula existe un grupo prioritario al aldehído, este pasa a ser un sustituyente que se nombra como oxo- o formil-.



Ácido 4-oxobutanoico

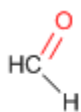


Ácido 3-formilciclohexanocarboxílico

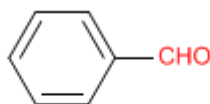
Tanto **-carbaldehído** como **formil-** son nomenclaturas que incluyen el carbono del grupo carbonilo. **-carbaldehído** se emplea cuando el aldehído es grupo funcional, mientras que **formil-** se usa cuando actúa de sustituyente.



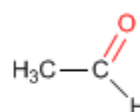
**Regla 4.** Algunos nombres comunes de aldehídos aceptados por la IUPAC son:



Formaldehído  
(Metanal)

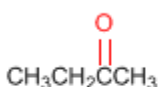


Benzaldehído  
(Benceno**carbaldehído**)

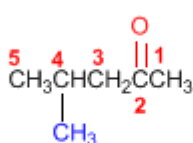


Acetaldehído  
(Etanal)

**Regla 5.** Las cetonas se nombran sustituyendo la terminación **-ano** del alcano con igual longitud de cadena por **-ona**. Se toma como cadena principal la de mayor longitud que contiene el grupo carbonilo y se numera para que éste tome el localizador más bajo.



Butan**ona**

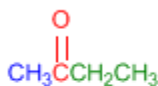


4-Metil-2-pentan**ona**

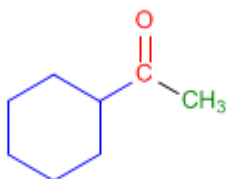


3-Metilciclohexan**ona**

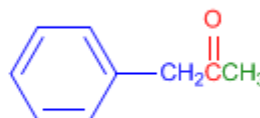
**Regla 6.** Existe un segundo tipo de nomenclatura para las cetonas, que consiste en nombrar las cadenas como sustituyentes, ordenándolas alfabéticamente y terminando el nombre con la palabra cetona.



Etil metil **cetona**

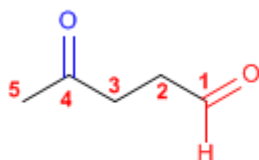


Ciclohexil metil **cetona**

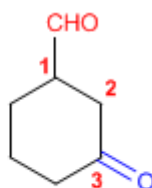


Fenil metil **cetona**

**Regla 7.** Cuando la cetona no es el grupo funcional de la molécula pasa a llamarse **OXO-**.



4-Oxopentan**al**

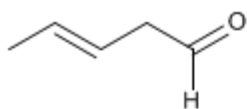


3-Oxociclohexano**carbaldehído**

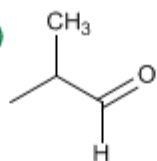
## Nomenclatura de Aldehídos y Cetonas - Problema 9.1

Nombra los siguientes aldehídos y cetonas:

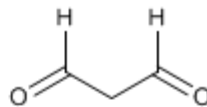
a)



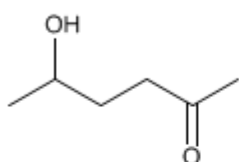
b)



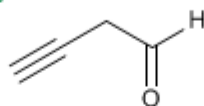
c)



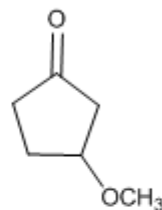
d)



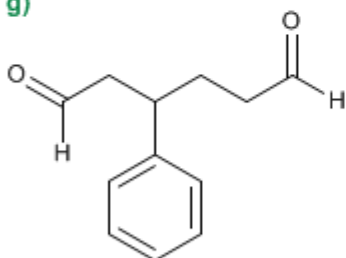
e)



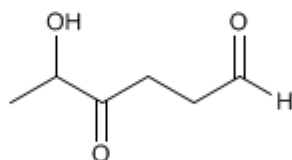
f)



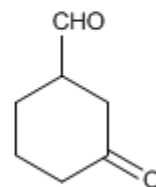
g)



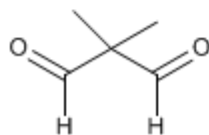
h)



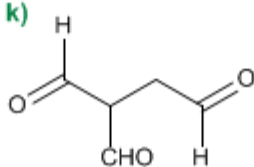
i)



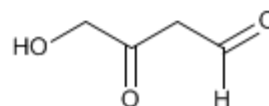
j)



k)

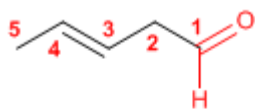


l)

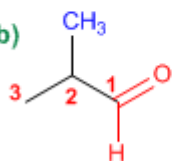


Solución

a)



b)



1. Cadena principal: 5 carbonos (pentano)

2. Numeración: comienza en el aldehído (grupo funcional)

Grupo funcional: aldehído

3. Nombre: Pent-3-enal

1. Cadena principal: 3 carbonos (propano)

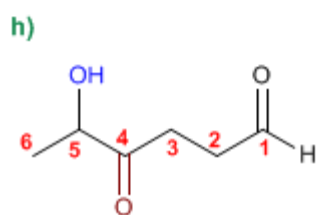
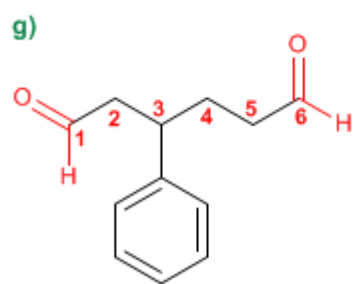
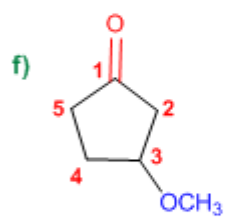
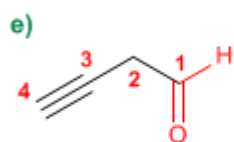
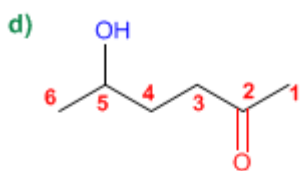
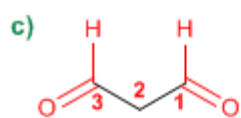
2. Numeración: localizador más bajo al aldehído.

3. Grupo funcional: aldehído

4. Sustituyentes: metilo en 2.

5. Nombre: 2-Metilpropanal

Los aldehídos y cetonas son prioritarios sobre alquenos y alquinos, y se numeran otorgándoles el localizador más bajo



1. Cadena principal: 3 carbonos (propano)
2. Grupo funcional: aldehído (dialdehído)
3. Nombre: Propanodial

1. Cadena principal: 6 carbonos (hexano)
2. Grupo funcional: cetona
3. Numeración: asignar el menor localizador a la cetona
4. Sustituyentes: hidroxí en 5.
5. Nombre: 5-Hidroxihexan-2-ona

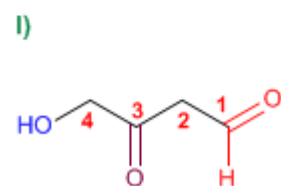
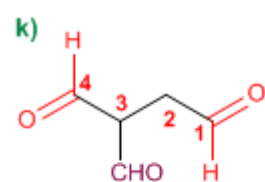
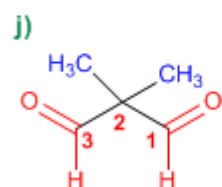
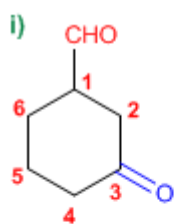
1. Cadena principal: 4 carbonos (butano)
2. Grupo funcional: aldehído
3. Numeración: asignar el menor localizador al aldehído
4. Nombre: But-3-inal

1. Cadena principal: ciclo de 5 miembros (ciclopentano)
2. Grupo funcional: cetona
3. Numeración: comienza en la cetona y prosigue hacia el sustituyente
4. Sustituyentes: metoxi en 3.
5. Nombre: 3-Metoxiciclopentanona

1. Cadena principal: 6 carbonos (hexano)
2. Grupo funcional: aldehído (dialdehído)
3. Numeración: comienza en el extremo que otorga al fenilo el localizador más bajo.
4. Sustituyentes: fenilo en 3.
5. Nombre: 3-Fenilhexanodial

1. Cadena principal: 6 carbonos (hexano)
2. Grupo funcional: aldehído
3. Numeración: asignar el menor localizador al aldehído
4. Sustituyentes: hidroxí en 5 y oxo en 4.
5. Nombre: 5-Hidroxí-4-oxohexanal

Los aldehídos son prioritarios sobre las cetonas que pasan a nombrarse como sustituyentes (oxo-)



1. Cadena principal: ciclo de 6 miembros (ciclohexano)
2. Grupo funcional: aldehído (-carbaldehído)
3. Numeración: menor localizador al grupo -CHO (este no se numera)
4. Sustituyentes: cetona (oxo-) en 3
5. Nombre: 3-Oxociclohexanocarbaldehído

1. Cadena principal: 3 carbonos (propano)
2. Grupo funcional: aldehído (dialdehído)
3. Sustituyentes: metilos en 2,2.
4. Nombre: 2,2-Dimetilpropanodial

1. Cadena principal: 4 carbonos (butano)
2. Grupo funcional: aldehído
3. Sustituyentes: formil en 3
4. Nombre: 3-Formilbutanodial

1. Cadena principal: 4 carbonos (butano)
2. Grupo funcional: aldehído
3. Numeración: asignar el menor localizador al aldehído
4. Sustituyentes: hidroxil en 4 y oxo en 3.
5. Nombre: 4-Hidroxil-3-oxobutanal

## Nomenclatura de Aldehídos y Cetonas - Problema 9.2

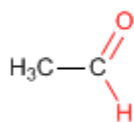
PRINT EMAIL

Dibuja la estructura de los siguientes aldehídos y cetonas:

- |   |                                  |
|---|----------------------------------|
| a) Etanal (acetaldehído)                          | g) 2,5-Dioxooctanodial           |
| b) 3-Metilbutanal                                 | h) 1,3-Ciclohexanodiona          |
| c) Benzaldehído                                   | i) 3-Metil-3-pental              |
| d) 4-Hidroxyciclohexanocarbaldehído               | j) 3-Oxobutanal                  |
| e) 3-Hidroxi-4-metil-5-oxociclohexanocarbaldehído | k) 3-Hidroxyciclopentanona       |
| f) 2-Metil-2,5-octanodiona                        | l) 4-Etoxi-5-fenil-3-oxoheptanal |

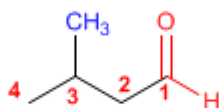
Solución

a)



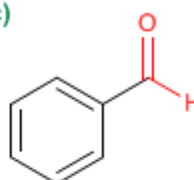
Etanal (acetaldehído)

b)

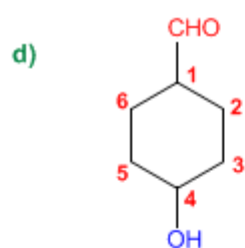


3-Metilbutanal

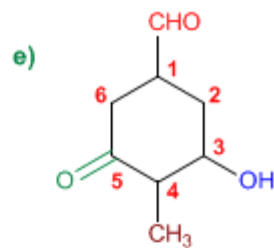
c)



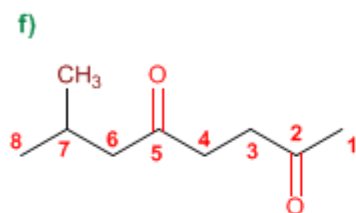
Benzaldehído



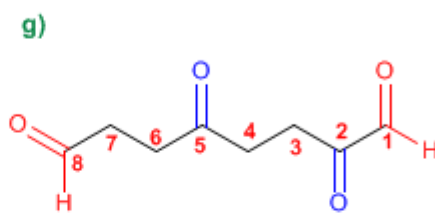
4-Hidroxiciclohexanocarbaldehído



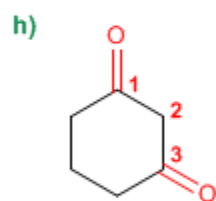
3-Hidroxi-4-metil-5-oxociclohexanocarbaldehído



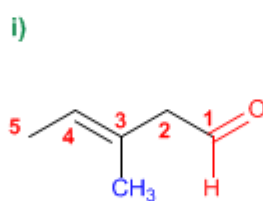
7-Metil-2,5-octanodiona



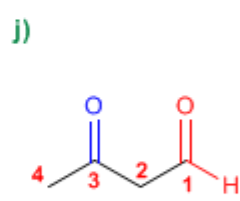
2,5-Dioxooctanal



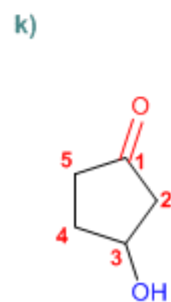
1,3-Ciclohexanodiona



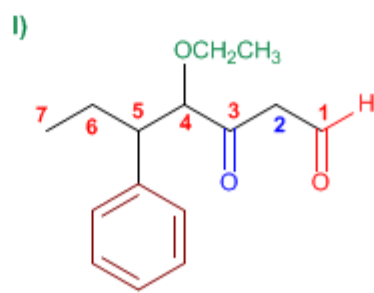
3-Metil-3-pentenal



3-Oxobutanal



3-Hidroxiciclopentanona



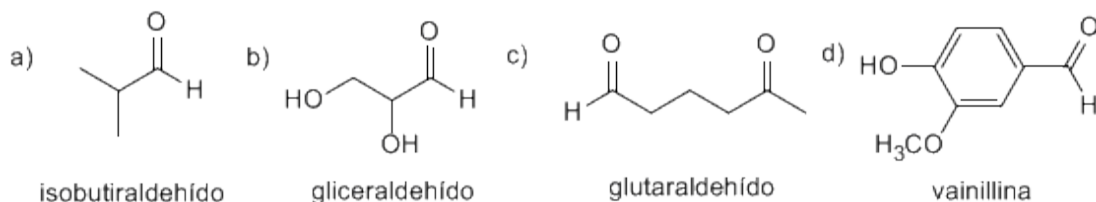
4-Etoxi-5-fenil-3-oxoheptanal



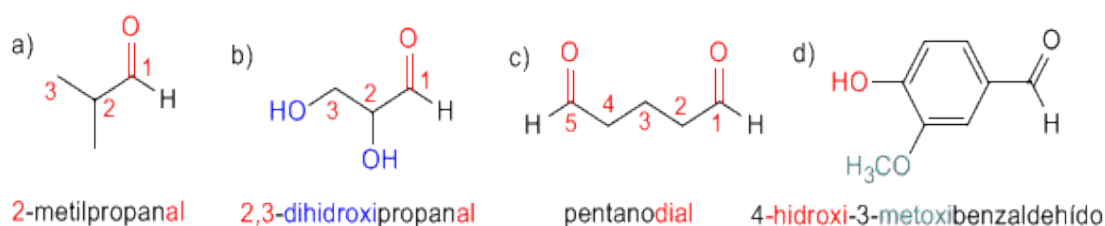
# PROBLEMAS RESUELTOS DE ALDEHÍDOS Y CETONAS

## Aldehídos y Cetonas: Problema 1

1) A continuación se dan nombres comunes y las fórmulas estructurales de algunos compuestos carbonílicos. Indique el nombre correspondiente según la IUPAC.



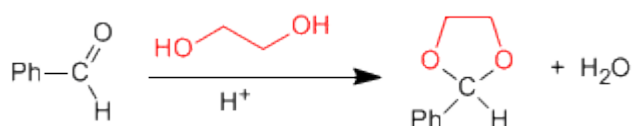
Solución



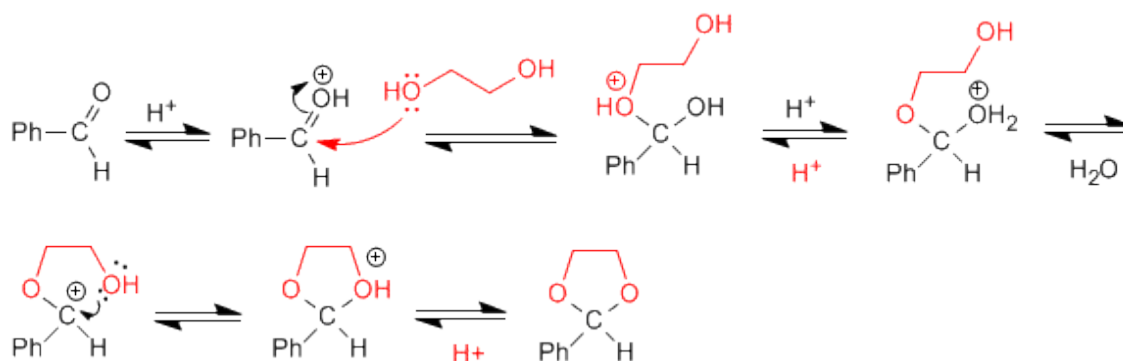
## Aldehídos y cetonas: Problema 2

Dibuje la estructura del acetal que se forma cuando el benzaldehído se calienta con 1,2-etanodiol en medio ácido. Escriba un mecanismo detallado que justifique su formación. Describa paso a paso la hidrólisis de este acetal en medio ácido acuoso.

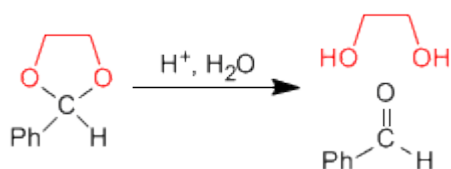
SOLUCIÓN



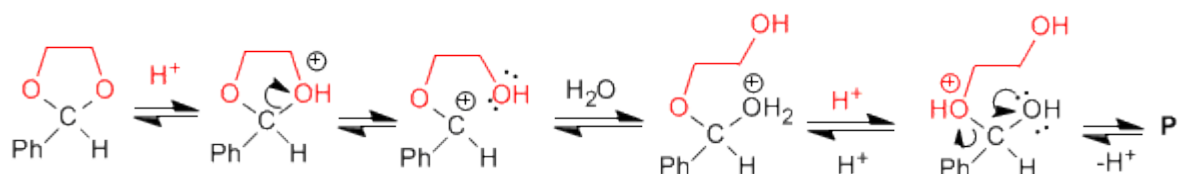
Mecanismo de formación del acetal:



La hidrólisis del acetal en medio ácido acuoso sigue es etapas inversas a la síntesis.



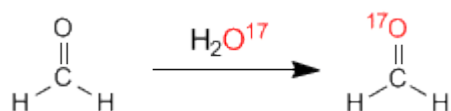
Mecanismo de hidrólisis del acetal cíclico.



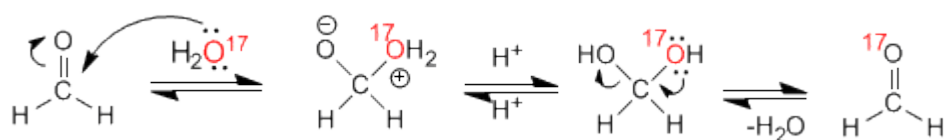
### Aldehídos y Cetonas: Problema 3

Cuando se disuelve formaldehído en agua marcada con  $^{17}\text{O}$ , se observa que después de unas horas tanto el hidrato del formaldehído como el formaldehído han incorporado el isótopo  $^{17}\text{O}$ . Sugiera una explicación razonable de este hecho.

SOLUCION



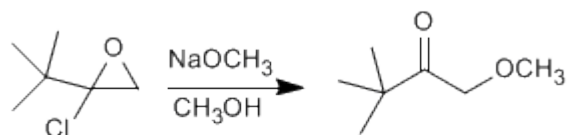
Mecanismo:



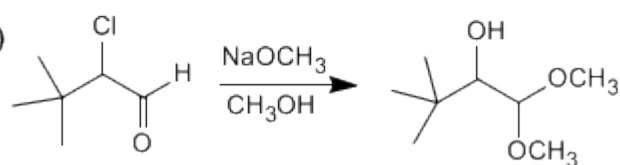
### Aldehídos y Cetonas: Problema 4

Sugiera un mecanismo razonable para una de las siguientes reacciones:

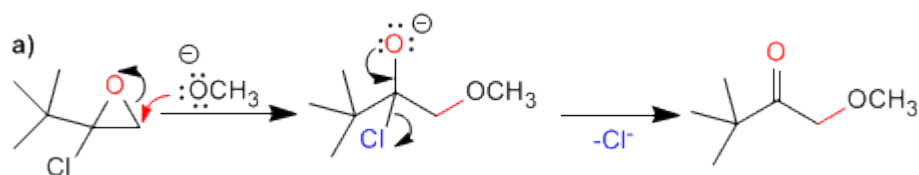
a)



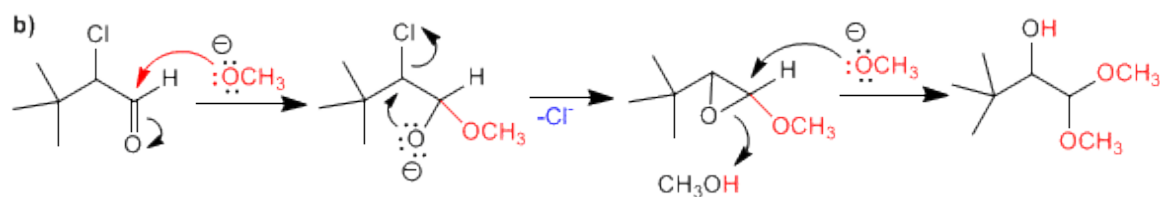
b)



## SOLUCION



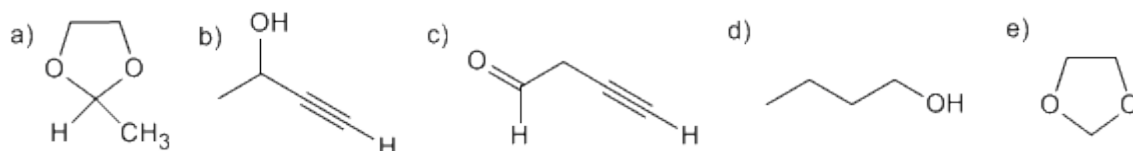
La primera etapa consiste en la apertura del oxaciclopropano sobre el carbono menos sustituido. En la segunda etapa, la cesión del par del oxígeno elimina el cloro, formándose un carbonilo.



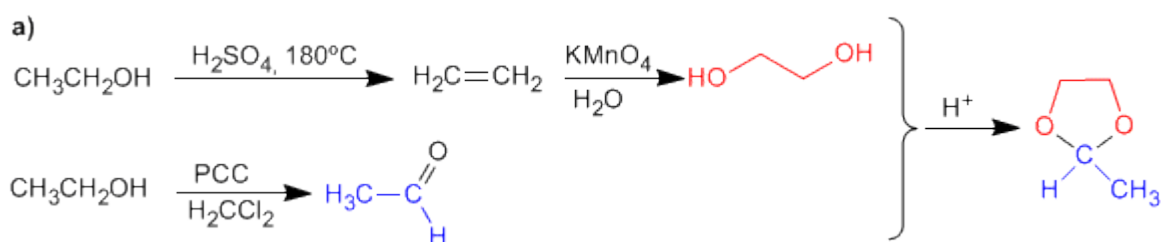
En el primer paso hay dos posibles posiciones de ataque; el carbono carbonilo y el carbono del cloro. Como el producto final no tiene metóxido en el carbono del cloro, atacamos al carbonilo. En la segunda etapa se produce una sustitución nucleófila intramolecular. Para terminar el metóxido abre el epóxido.

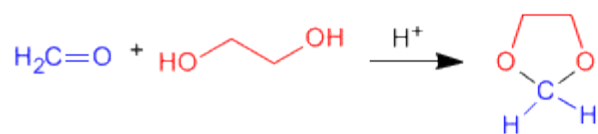
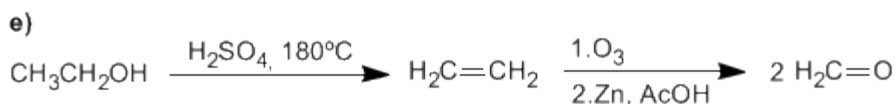
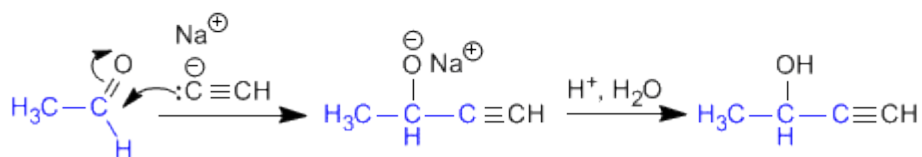
## Aldehídos y Cetonas: Problema 5

Usando etanol como fuente de todos los átomos de carbono y los reactivos que necesite, describa una síntesis eficiente de cada una de las sustancias siguientes:

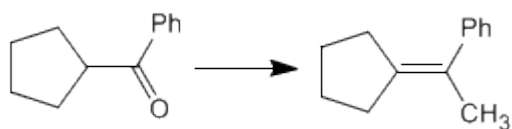


## SOLUCIÓN





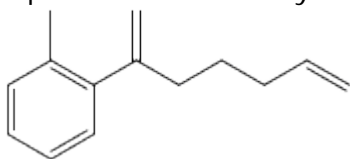
Utilizando los reactivos necesarios, indicar las etapas que permiten realizar la siguiente transformación:



[2] Isomerización en medio ácido, impulsada por la mayor estabilidad del alqueno interno.

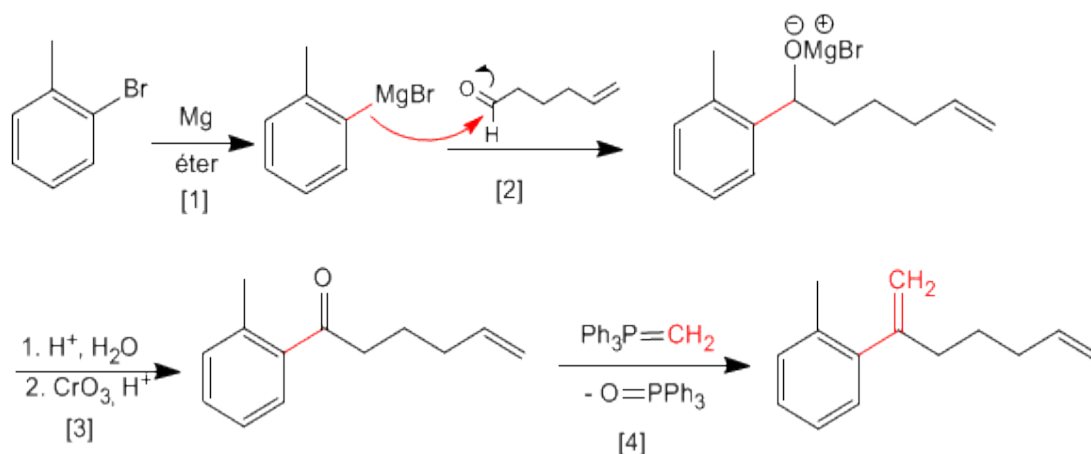
## Aldehídos y Cetonas: Problema 7

A partir de 5-hexenal y o-bromotolueno obtener el siguiente producto.



Pueden ser necesarios reactivos orgánicos e inorgánicos adicionales.

SOLUCIÓN



[1] Formación del magnesiano

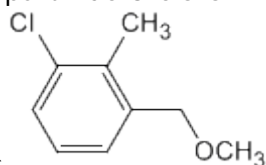
[2] Ataque nucleófilo del magnesiano al carbonilo.

[3] Hidrólisis y posterior oxidación del alcohol secundario.

[4] Reacción de Wittig entre la cetona y el trifenilmetilenfosforano.

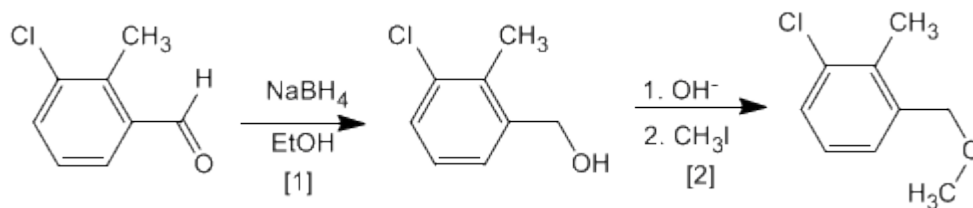
## Aldehídos y Cetonas: Problema 8

Obtener a partir de 3-cloro-2-metilbenzaldehído y de los reactivos



necesarios  
el compuesto siguiente:

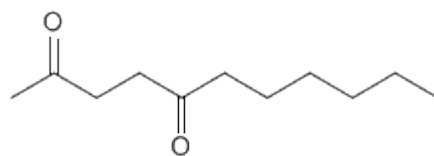
SOLUCIÓN



[1] Reducción del aldehído a alcohol

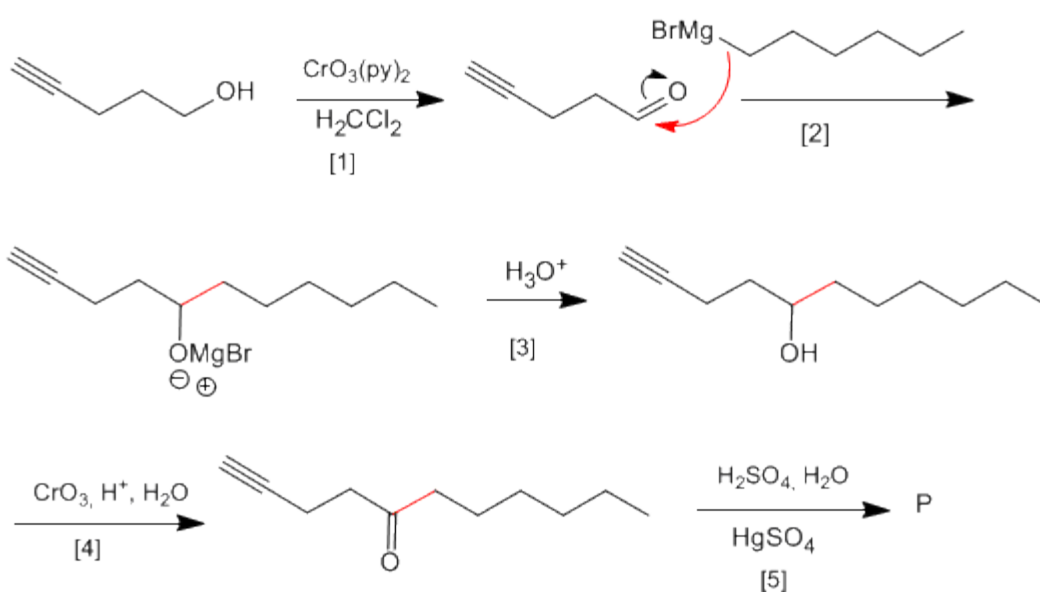
[2] Síntesis de Williamson de éteres.

## Aldehídos y Cetonas: Problema 9



A partir de 4-pentin-1-ol obtener:

SOLUCIÓN

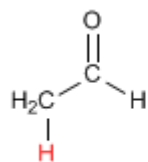


- [1] Oxidación del alcohol a aldehído
- [2] Formación del enlace carbono-carbono mediante organometálicos de magnesio
- [3] Protonación del alcohol
- [4] Oxidación del alcohol con Jones (Puedes utilizar también  $\text{CrO}_3(\text{py})_2$ )
- [5] Hidratación Markovnikov del alquino, para formar cetonas

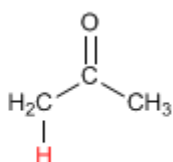
# TEORÍA DE ENOLES Y ENOLATOS

## Formación de Enolatos

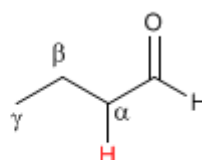
Los aldehídos y cetonas presentan hidrógenos ácidos en la posición vecina al grupo carbonilo, conocida como posición alfa. Estos hidrógenos presentan un pKa comprendido entre 18 y 21.



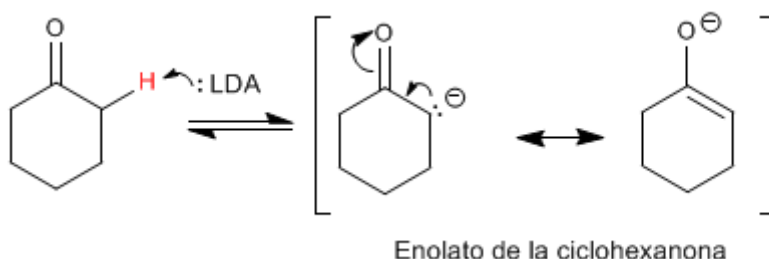
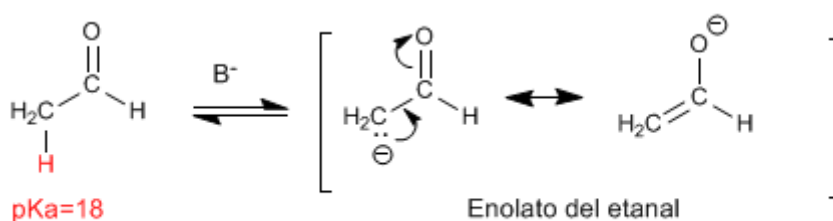
pKa=18



pKa=20-21



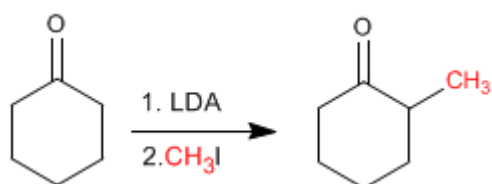
La acidez de los hidrógenos  $\alpha$  es debida a la estabilización de la base conjugada (enolato) por resonancia.



## Alquilación de Enolatos

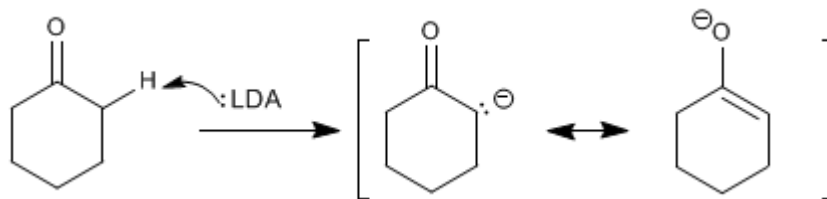
Los enolatos actúan como nucleófilos a través del carbono atacando a un gran número de electrófilos (haloalcanos, epóxidos, carbonilos, ésteres.....). En este punto nos fijaremos en la reacción entre enolatos y haloalcanos, que permite añadir cadenas carbonadas a la posición  $\alpha$  de la cadena.

La Ciclohexanona se convierte en 2-Metilciclohexanona por tratamiento con LDA seguido de yoduro de metilo.

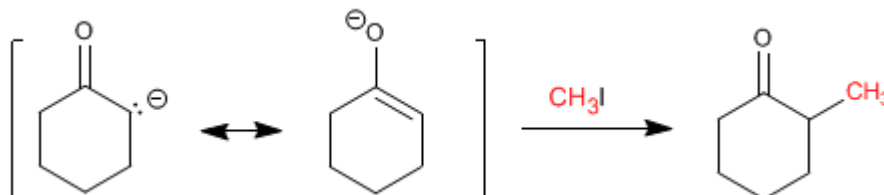


Etapas del mecanismo por el que se alquila la ciclohexanona:

**Etapas 1.** Formación del enolato

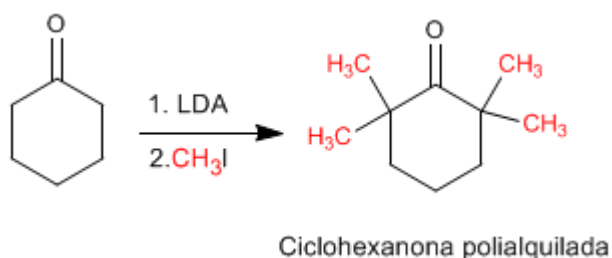


**Etapas 2.** Ataque nucleófilo del enolato sobre el haloalcano (Reacción de tipo S<sub>N</sub>2)



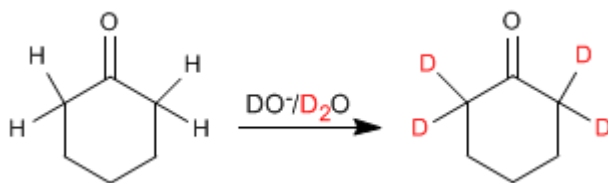
Las reacciones de alquilación tienen dos importantes problemas.

1. Competencia con la condensación aldólica. Los carbonilos en medio básico tienden a condensar para formar aldoles.
2. La reacción es difícil de controlar y tiende a polialquilar el carbonilo.



## Intercambio hidrógeno - Deuterio

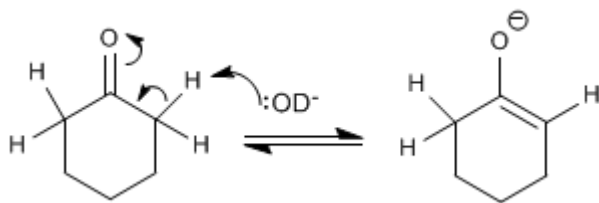
Los aldehídos y cetonas intercambian sus hidrógenos  $\alpha$  por deuterios cuando se tratan con  $\text{DO}^-/\text{D}_2\text{O}$  o con  $\text{D}^+/\text{D}_2\text{O}$ . En medios básicos la reacción transcurre a través de enolatos y en medios ácidos los intermediarios formados son enoles.



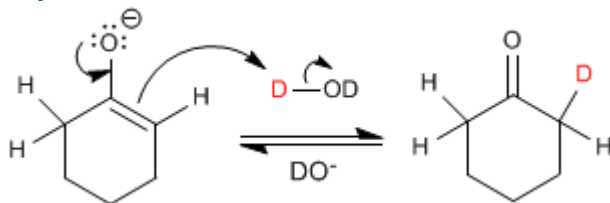
El mecanismo del intercambio hidrógeno-deuterio transcurre en los siguientes pasos:

**Etapas 1.** Formación del enolato

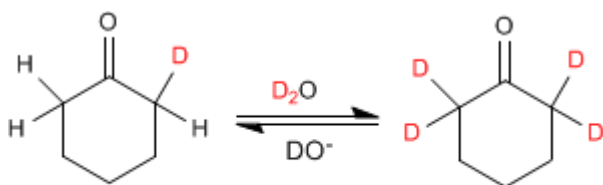




**Etapas 2.** Transferencia del deuterio al enolato



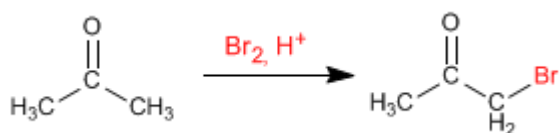
**Etapas 3.** Sustitución del resto de hidrógenos



## Halogenación de aldehídos y cetonas

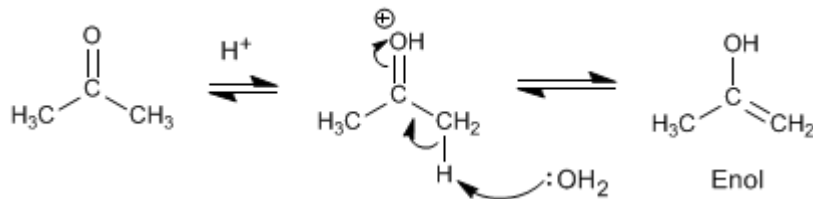
Los aldehídos y cetonas reaccionan con halógenos en medios ácidos o básicos produciéndose la sustitución de hidrógenos  $\alpha$  por halógenos.

Halogenación de la propanona en medio ácido:

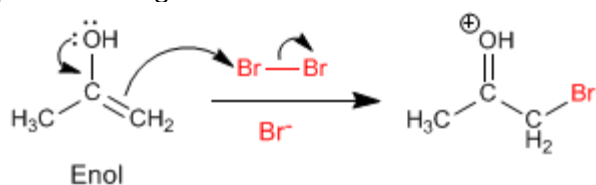


El mecanismo de halogenación en **medio ácido** tiene las siguientes etapas:

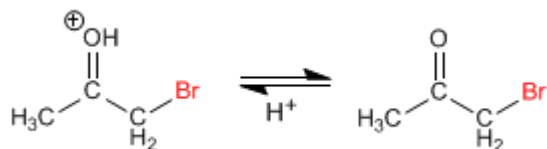
**Etapas 1.** Formación del enol



**Etapas 2.** Ataque nucleófilo del enol sobre el halógeno ayudado por la cesión del para del oxígeno.

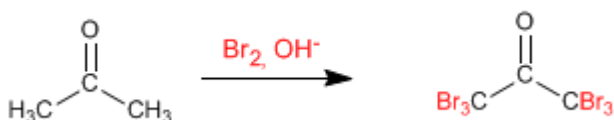


### Etapa 3. Desprotonación



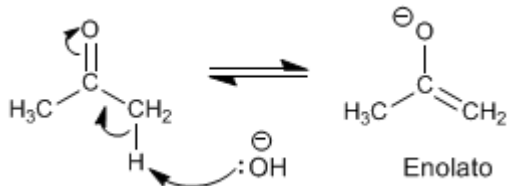
Trabajando con un equivalente de reactivo la halogenación para en una primera adición y no ocurren polihalogenaciones. El paso clave del mecanismo es la formación del enol y esta etapa requiere protonar el oxígeno del carbonilo. Una vez halogenada la posición  $\alpha$  al oxígeno se vuelve menos básico, debido al efecto electronegativo del bromo, protonándose peor.

Halogenación de la propanona en **medio básico**:

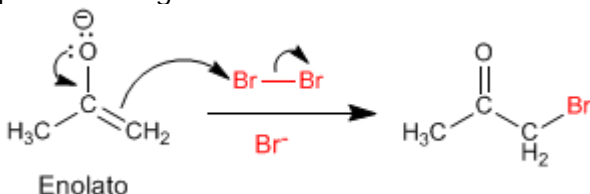


La halogenación en medio básico tiene el siguiente mecanismo:

### Etapa 1. Formación del enolato



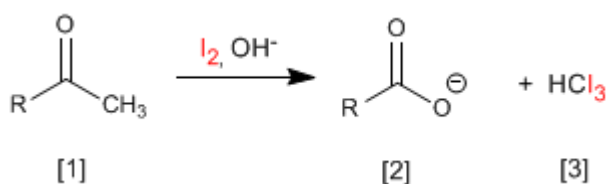
**Etapa 2.** Ataque nucleófilo del enolato sobre el halógeno ayudado por la cesión del par del oxígeno.



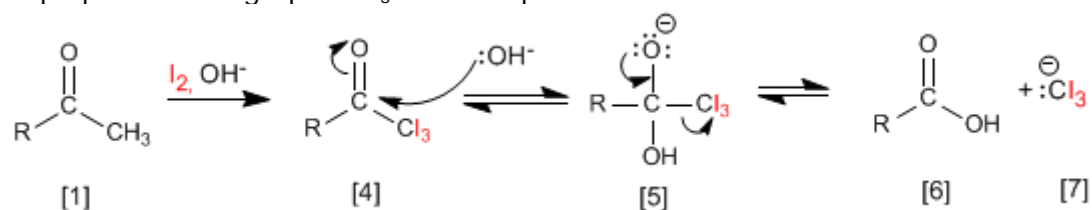
Este mecanismo se repite otras 5 veces sustituyendo todos los hidrógenos  $\alpha$  por halógenos. En este caso la reacción no para puesto que el producto halogenado es más reactivo que la propanona de partida. La base arranca mejor los hidrógenos en el producto halogenado (son más ácidos), haciendo imposible parar la reacción.

## Reacción del Haloformo (Yodoformo)

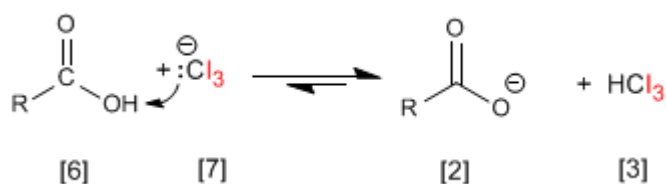
Las cetonas metílicas [1] reaccionan con halógenos en medios básicos generando carboxilatos [2] y haloformo [3].



El mecanismo consiste en halogenar completamente el metilo, sustituyendo en una etapa posterior el grupo -CX<sub>3</sub> formado por -OH.



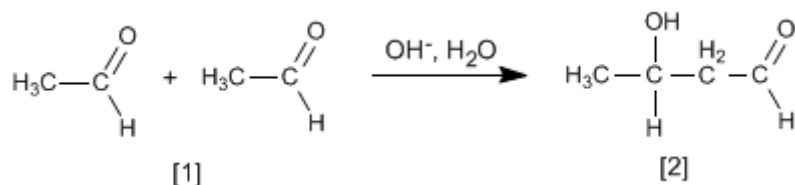
El grupo Cl<sub>3</sub><sup>-</sup> es muy básico y desprotona el ácido carboxílico formándose yodoformo y el carboxilato.



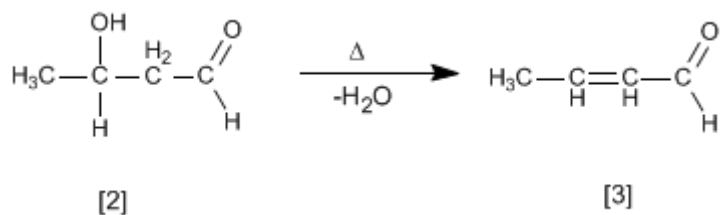
Esta reacción (con yodo) puede emplearse como ensayo analítico para identificar cetonas metílicas aprovechando que el yodoformo precipita de color amarillo.

## Condensación Aldólica

Aldehídos y cetonas [1] condensan en medios básicos formando aldoles [2]. Esta reacción se denomina condensación aldólica.

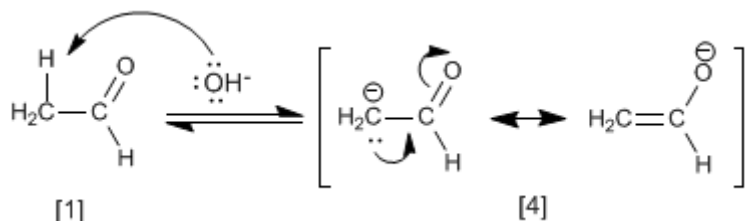


El aldol [2] formado deshidrata en el medio básico por calentamiento para formar un α,β-insaturado [3].



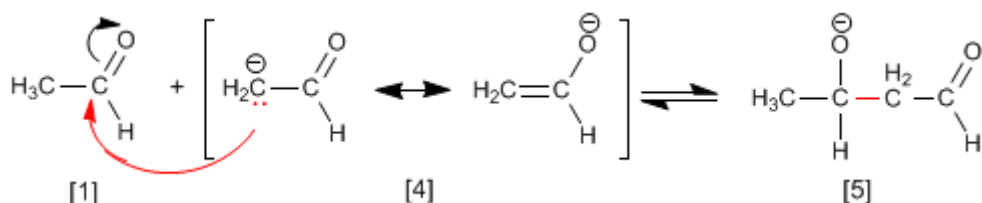
El mecanismo de la condensación aldólica transcurre con formación de un enolato, que ataca al carbonilo de otra molécula. En esta condensación se forma un enlace carbono-carbono entre el carbonilo de una molécula y el carbono  $\alpha$  de la otra.

### Etapas 1. Formación del enolato

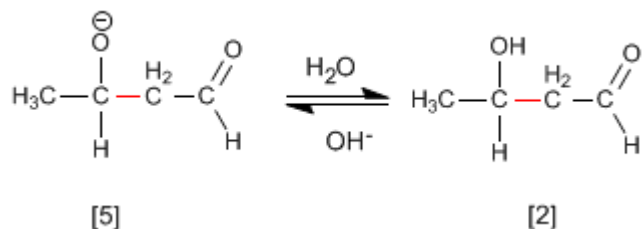


La base desprotona el carbono alfa del etanal [1] generando el enolato [4] estabilizado por resonancia.

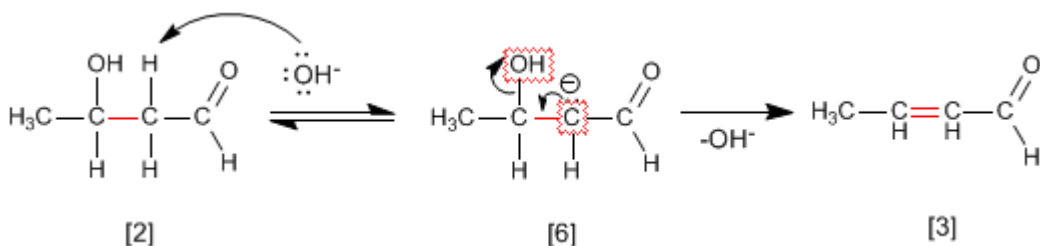
### Etapas 2. Ataque nucleófilo del enolato sobre el carbonilo



### Etapas 3. Protonación

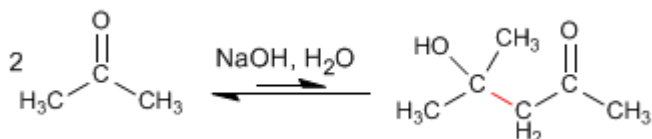


### Etapas 4. Deshidratación del aldol

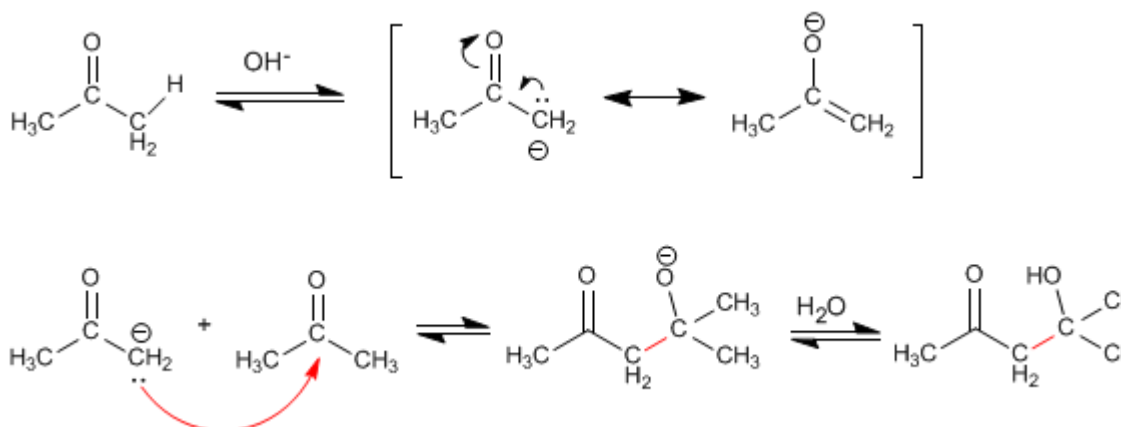


## Condensación aldólica con cetonas

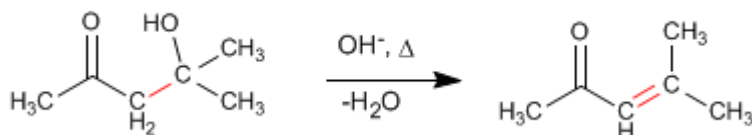
Las cetonas son menos reactivas que los aldehídos y dan un rendimiento muy bajo en la condensación aldólica. Así, dos moléculas de propanona condensan para formar el aldol correspondiente con un rendimiento del 2%. Se pueden conseguir porcentajes elevados del producto separándolo del medio de reacción según se va formando, o bien, calentando para deshidratarlo. De ambas formas los equilibrios de la aldólica se desplazan hacia el producto final.



**Mecanismo de la reacción:**

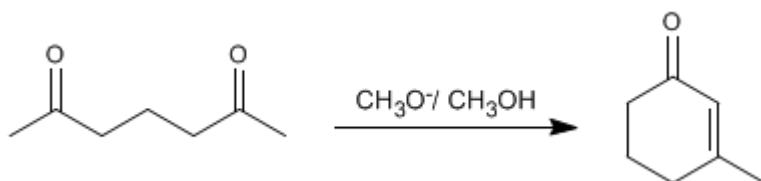


La deshidratación final permite el desplazamiento de los equilibrios. También se puede realizar una extracción del aldol del medio de reacción para favorecer la reacción.



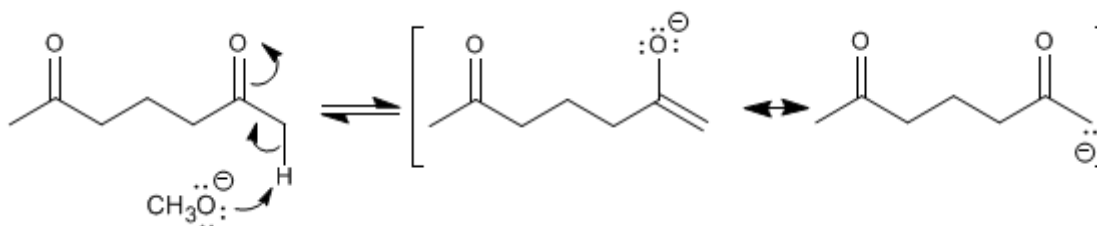
## Condensación aldólica intramolecular

Los compuestos dicarbonílicos condensan mediante la aldólica intramolecular en medios básicos. En esta reacción se obtienen ciclos de cinco o seis miembros. Así, la 2,6-heptanodiona condensa con metóxido en metanol para formar el 3-metilciclohex-2-enona.

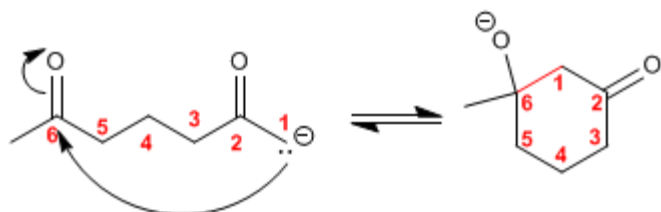


El mecanismo de la reacción transcurre a través de las siguientes etapas:

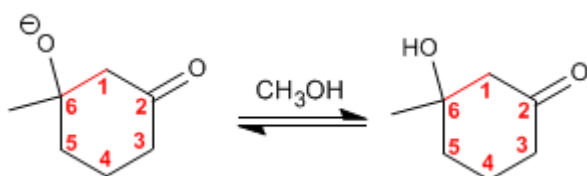
### Etapa 1. Formación del enolato.



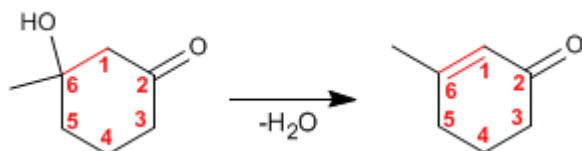
### Etapa 2. Adición nucleófila intramolecular



### Etapa 3. Protonación de la base del aldol



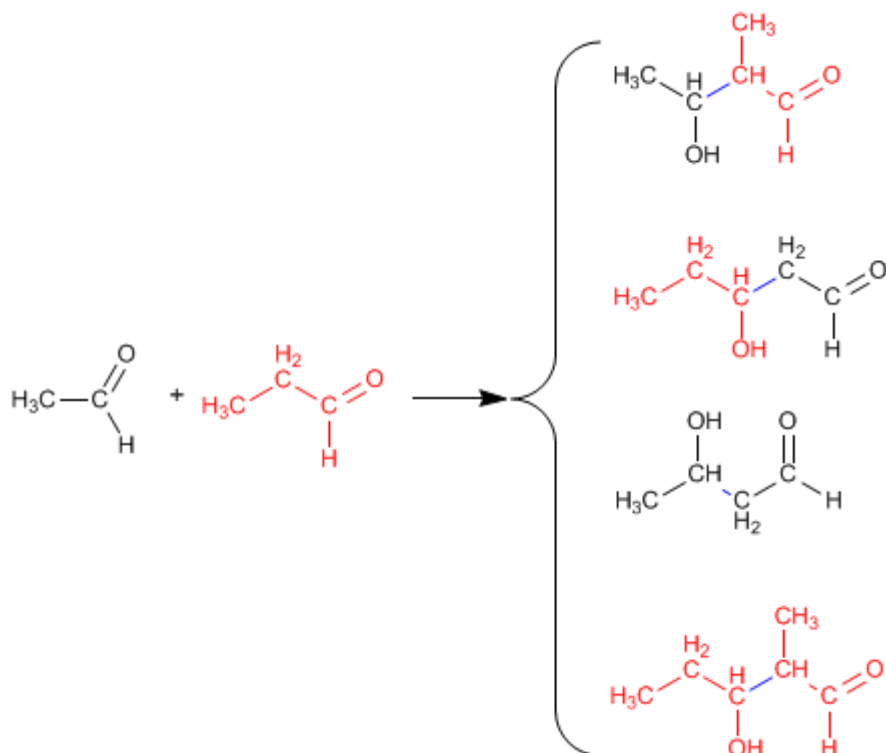
### Etapa 4. Deshidratación del aldol



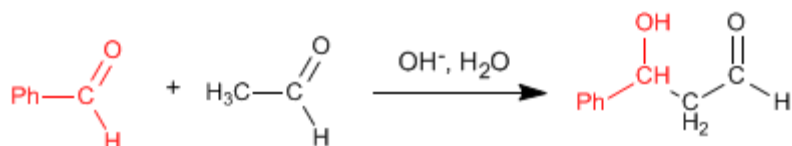
## Condensación aldólica cruzada o mixta

La reacción entre dos carbonilos diferentes se llama aldólica cruzada o mixta. Esta reacción sólo tiene utilidad sintética en dos casos:

1. Sólo uno de los carbonilos puede formar enolatos.
  2. Uno de los carbonilos es mucho más reactivo que el otro.
- En el resto de situaciones la aldólica mixta genera mezclas de cuatro productos. Veamos como ejemplo la condensación del etanal y propanal.

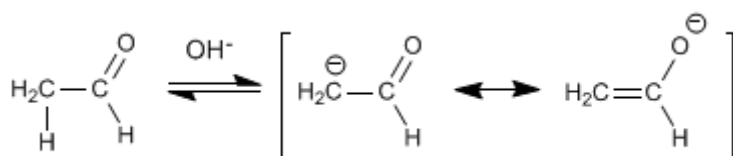


La condensación aldólica mixta del etanal con el benzaldehído genera un producto, cuando se trabaja en exceso de benzaldehído, debido a que el benzaldehído carece de hidrógenos en el carbono alfa y no puede formar enolatos.



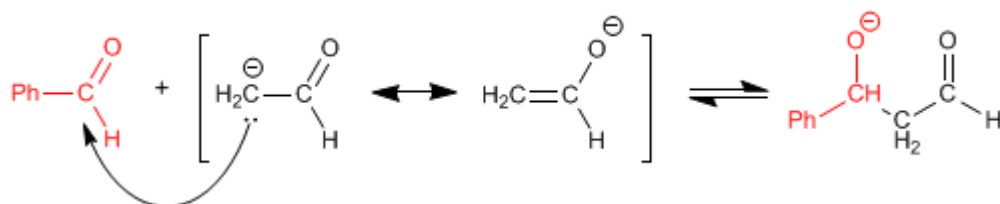
El mecanismo de esta reacción tiene lugar en las siguientes etapas:

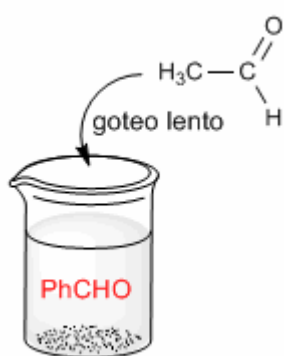
**Etapas 1.** Enolización del etanal



La formación de enolatos sólo puede tener lugar con el etanal, puesto que el benzaldehído carece de hidrógenos ácidos en el carbono alfa.

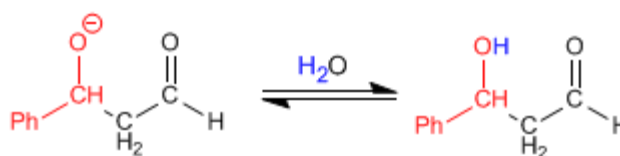
**Etapas 2.** Ataque nucleófilo del enolato al benzaldehído.





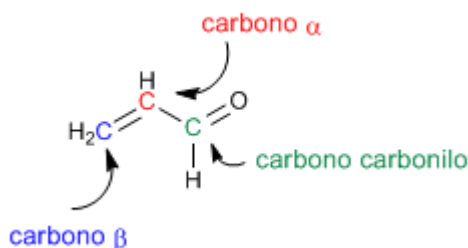
En esta etapa puede ocurrir el ataque del enolato de etanal sobre si mismo. Para evitarlo debe trabajarse en exceso de benzaldehído. Un procedimiento experimental muy usado para evitar la condensación del etanal consigo mismo es gotear lentamente el etanal sobre una disolución básica de benzaldehído

### Etapa 3. Protonación



## Síntesis de carbonilos alfa,beta-insaturados

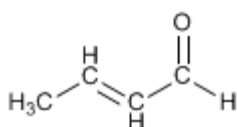
Los carbonilos  $\alpha,\beta$ -insaturados son compuestos orgánicos que tienen un doble enlace entre las posiciones  $\alpha,\beta$  de un aldehído o cetona.



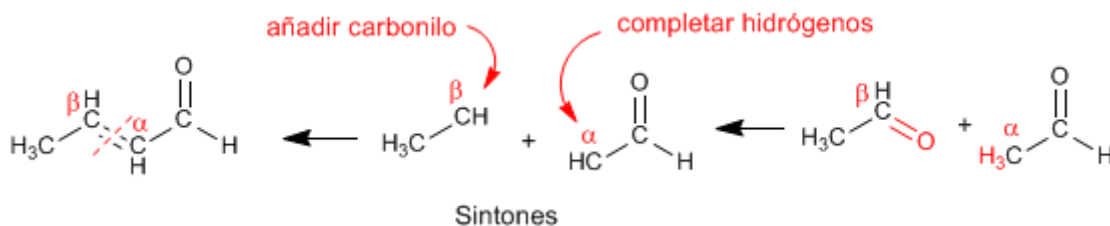
El propenal o acroleína es un carbonilo  $\alpha,\beta$ -insaturado. Sus dos dobles enlaces conjugados le confieren una reactividad especial.

Existen 4 métodos importantes para la preparación de  $\alpha,\beta$ -insaturados: condensación aldólica, halogenación del carbono  $\alpha$  seguida de eliminación, oxidación de alcoholes alílicos y Wittig.

**Método 1.** Preparar mediante la condensación aldólica el siguiente compuesto.



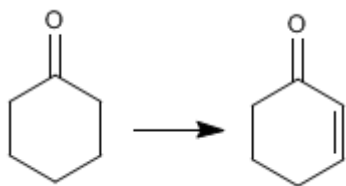
Empleamos la retrosíntesis para preparar el compuesto. Al ser de la familia de los  $\alpha,\beta$ -insaturados se puede obtener mediante la condensación aldólica.



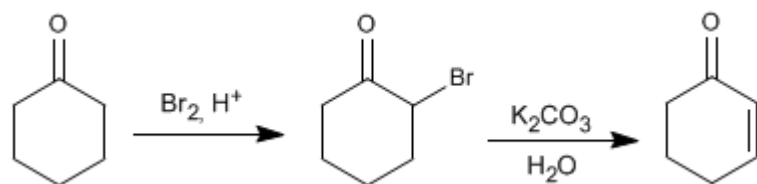
Para obtener los reactivos que forman el  $\alpha,\beta$ -insaturado se rompe por el doble enlace, obteniéndose los sintones (equivalentes sintéticos). Los reactivos se obtienen añadiendo al carbono  $\beta$  un carbonilo y completando los hidrógenos que faltan en el carbono  $\alpha$ .



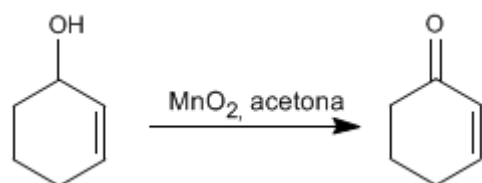
**Ejemplo 2.** Indicar como se puede realizar las siguiente transformación.



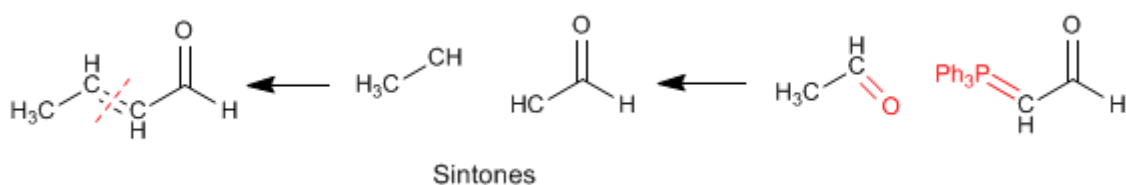
En una primera etapa se halogena la posición  $\alpha$  del carbonilo. En la segunda etapa se realiza una eliminación que nos deja el producto final.



**Método 3.** La oxidación de alcoholes alílicos con dióxido de manganeso en acetona produce  $\alpha,\beta$ -insaturados

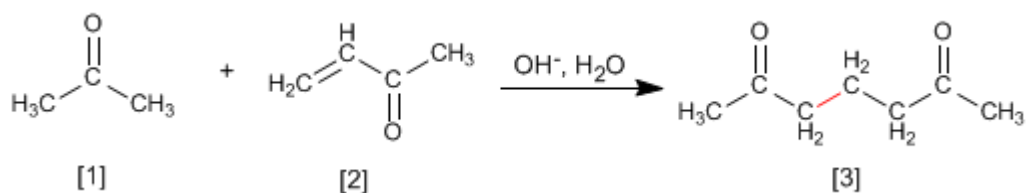


**Método 4.** Reacción de Wittig



## Adición de Michael y anelación de Robinson

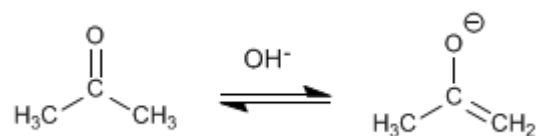
Los enolatos de aldehídos o cetonas se adicionan a los  $\alpha,\beta$ -insaturados para formar 1,5-dicarbonilos. Esta reacción se denomina adición de Michael.



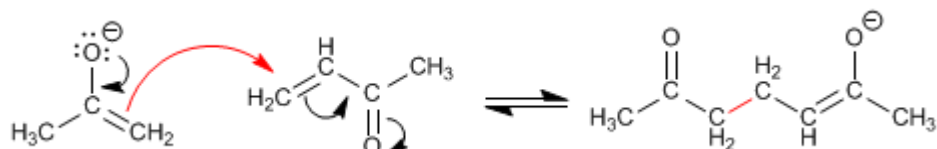
La propanona [1] reacciona con el  $\alpha,\beta$ -insaturado [2] para formar el 1,5-dicarbonilo [3]

Mecanismo de la Adición de Michael:

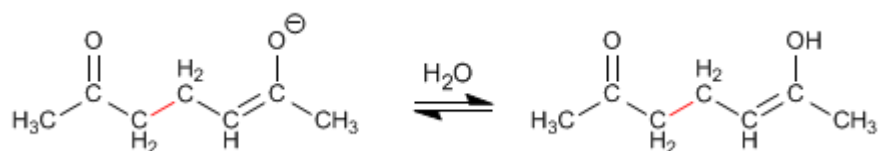
**Etapla 1.** Formación del enolato.



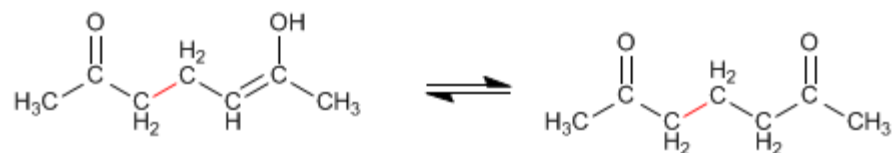
**Etapla 2.** Ataque nucleófilo del enolato al carbono  $\beta$  del  $\alpha,\beta$ -insaturado.



**Etapla 3.** Equilibrio ácido-base



**Etapla 4.** Tautomería ceto-enol



El producto de Michael puede condensar mediante una aldólica intramolecular, formando un  $\alpha,\beta$ -insaturado. El conjunto de la adición de Michael y la aldólica final se conoce como reacción de Robinson

*Chemsoft ®*

# *Química Orgánica*

*Recopilación : 2da Edición - 2009*

*José A.*

# *Química Orgánica*

*Recopilación: 2da Edición*

*Diciembre 2009*

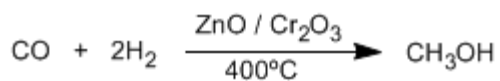
## *Índice:*

- i. Alcoholes*
- ii. Éteres*
- iii. Aldehídos y Cetonas*
- iv. Enoles y Enolatos*
- v. Benceno*

## SÍNTESIS Y REACTIVIDAD DE ALCOHOLES

### Alcoholes - características generales

Los alcoholes son compuesto orgánicos que contienen el grupo hidroxilo (-OH). El metanol es el alcohol más sencillo, se obtiene por reducción del monóxido de carbono con hidrógeno.

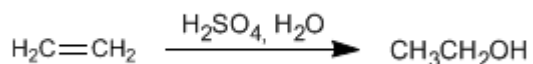


El metanol es un líquido incoloro, su punto de ebullición es 65°C, miscible en agua en todas las proporciones y venenoso (35 ml pueden matar una persona)

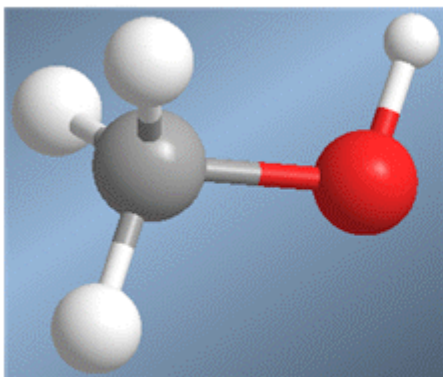
La mitad del metanol producido se oxida a metanal (formaldehído), material de partida para la fabricación de resinas y plásticos.

El etanol se obtiene por fermentación de materia vegetal, obteniéndose una concentración máxima de 15% en etanol. Por destilación se puede aumentar esta concentración hasta el 98%.

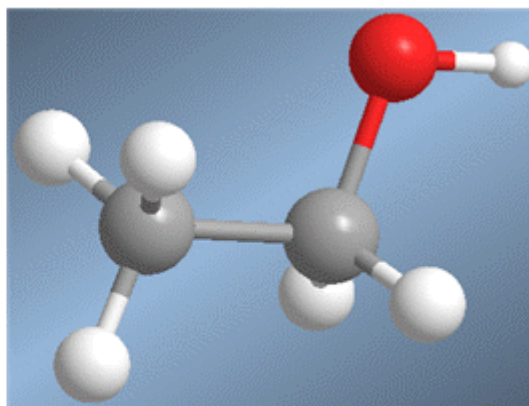
También se puede obtener etanol por hidratación del etileno (eteno) que se obtiene a partir del petróleo.



El etanol es un líquido incoloro, miscible en agua en todas proporciones, con punto de ebullición de 78°C. Es fácilmente metabolizado por nuestros organismos, aunque su abuso causa alcoholismo.



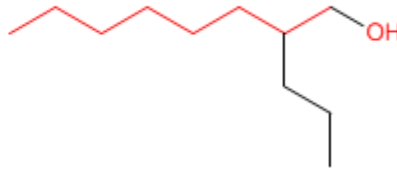
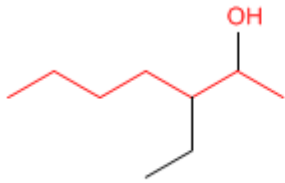
(metanol)  $\text{CH}_3\text{OH}$



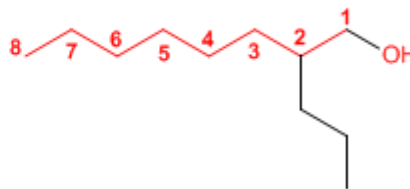
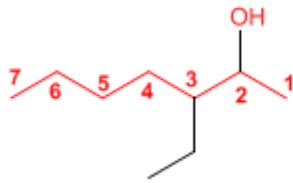
(etanol)  $\text{CH}_3\text{CH}_2\text{OH}$

## Nomenclatura de Alcoholes

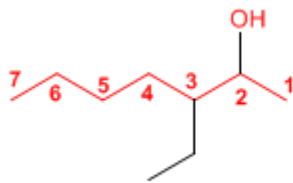
**Regla 1.** Se elige como cadena principal la de mayor longitud que contenga el grupo -OH.



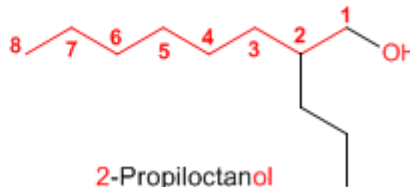
**Regla 2.** Se numera la cadena principal para que el grupo -OH tome el localizador más bajo. El grupo hidroxilo tiene preferencia sobre cadenas carbonadas, halógenos, dobles y triples enlaces.



**Regla 3.** El nombre del alcohol se construye cambiando la terminación -o del alcano con igual número de carbonos por -ol

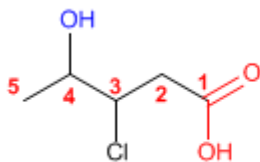


3-Etilheptanol

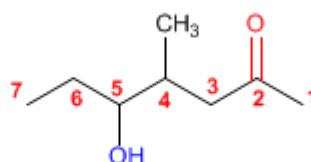


2-Propiloctanol

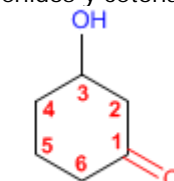
**Regla 4.** Cuando en la molécula hay grupos funcionales de mayor prioridad, el alcohol pasa a ser un mero sustituyente y se llama **hidroxi-**. Son prioritarios frente a los alcoholes: ácidos carboxílicos, anhídridos, ésteres, haluros de alcanoilo, amidas, nitrilos, aldehídos y cetonas.



Ácido 3-cloro-4-hidroxi-pentanoico

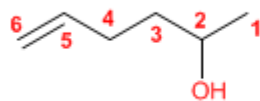


5-Hidroxi-4-metilheptanona

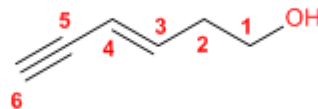


3-Hidroxiciclohexanona

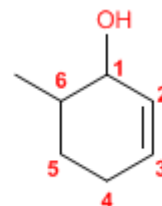
**Regla 5.** El grupo -OH es prioritario frente a los alquenos y alquinos. La numeración otorga el localizador más bajo al -OH y el nombre de la molécula termina en -ol.



Hex-5-en-2-ol



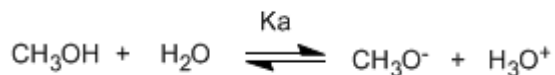
Hex-3-en-5-in-1-ol



6-Metilciclohex-2-en-1-ol

## Acidez y basicidad de alcoholes

Los alcoholes son especies anfóteras (anfipróticas), pueden actuar como ácidos o bases. En disolución acuosa se establece un equilibrio entre el alcohol, el agua y sus bases conjugadas.



Escribiendo la constante del equilibrio ( $K_a$ )

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{CH}_3\text{O}^-]}{[\text{CH}_3\text{OH}]} = 10^{-15.5}$$

El pequeño valor de la constante nos indica que el equilibrio está totalmente desplazado a la izquierda.

El logaritmo cambiado de signo de la constante de equilibrio nos da el  $pK_a$  del metanol, parámetro que indica el grado de acidez de un compuesto orgánico.

$$pK_a = -\log k_a = 15.5$$

El aumento del  $pK_a$  supone una disminución de la acidez. Así, el metanol con un  $pK_a$  de 15.5 es ligeramente más ácido que el etanol con  $pK_a$  de 15.9.

El  $pK_a$  de los alcoholes se ve influenciado por algunos factores como son el tamaño de la cadena carbonada y los grupos electronegativos

Al aumentar el tamaño de la cadena carbonada el alcohol se vuelve menos ácido.

$\text{CH}_3\text{OH}$	$pK_a = 15.5$	
$\text{CH}_3\text{CH}_2\text{OH}$	$pK_a = 15.9$	
$(\text{CH}_3)_2\text{CHOH}$	$pK_a = 17.1$	
$(\text{CH}_3)_3\text{COH}$	$pK_a = 18$	

Los grupos electronegativos (halógenos) aumentan la acidez de los alcoholes (bajan el  $pK_a$ )

$\text{CH}_3\text{CH}_2\text{OH}$	$pK_a = 15.9$	
$\text{ClCH}_2\text{CH}_2\text{OH}$	$pK_a = 14.3$	
$\text{F}_3\text{CCH}_2\text{OH}$	$pK_a = 12.4$	

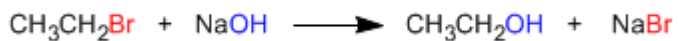


## Síntesis de Alcoholes a partir de Haloalcanos

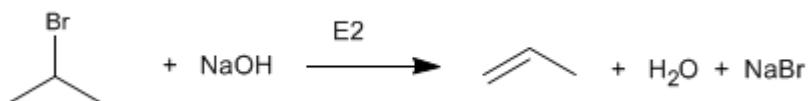
Los alcoholes se pueden obtener a partir de haloalcanos mediante reacciones  $S_N2$  y  $S_N1$

### Síntesis de alcoholes mediante $S_N2$

Los haloalcanos primarios reaccionan con hidróxido de sodio para formar alcoholes. Haloalcanos secundarios y terciarios eliminan para formar alquenos.

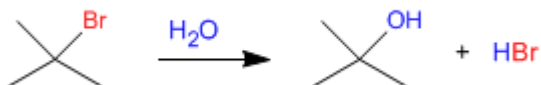


El bromuro de isopropilo (sustrato secundario) elimina al reaccionar con el ión hidróxido.



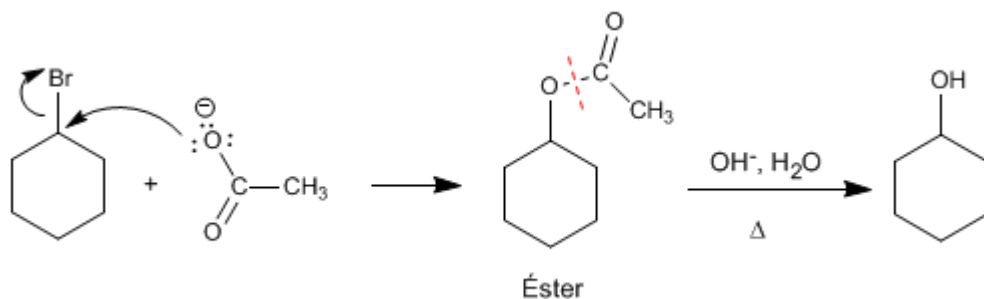
### Síntesis de alcoholes mediante $S_N1$

Los sustratos secundarios y terciarios reaccionan con agua mediante mecanismo  $S_N1$  para formar alcoholes.



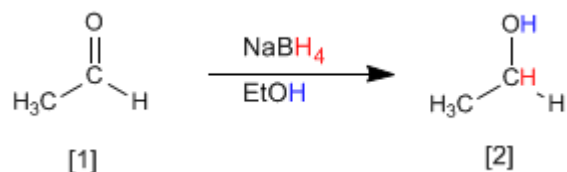
### Hidrólisis de ésteres

Es un método interesante para preparar alcoholes a partir de haloalcanos secundarios. El haloalcano se convierte en éster por reacción con acetato de sodio, para después hidrolizarse en medio ácido o básico, obteniéndose el alcohol.



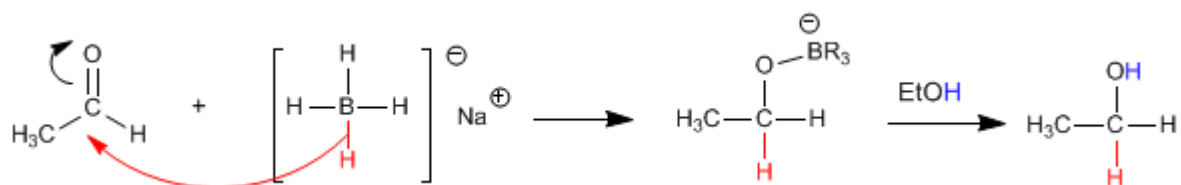
## Síntesis de Alcoholes por reducción de carbonilos

Tanto el borohidruro de sodio ( $\text{NaBH}_4$ ) como el hidruro de litio y aluminio ( $\text{LiAlH}_4$ ) reducen aldehídos y cetonas a alcoholes.

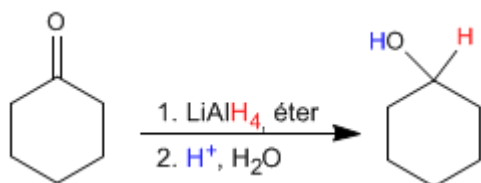


El etanal [1] se transforma por reducción con el borohidruro de sodio en etanol [2].

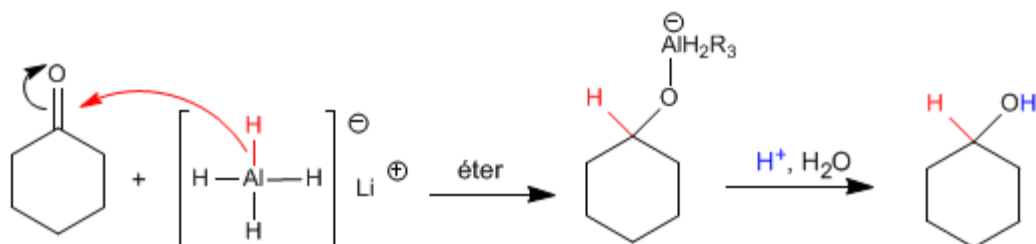
El mecanismo transcurre por ataque del hidruro procedente del reductor sobre el carbono carbonilo. En una segunda etapa el disolvente protona el oxígeno del alcóxido.



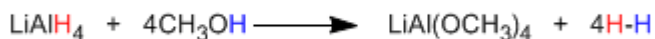
El hidruro de litio y aluminio trabaja en medio éter y transforma aldehídos y cetonas en alcoholes después de una etapa de hidrólisis ácida.



El mecanismo es análogo al del borohidruro de sodio.



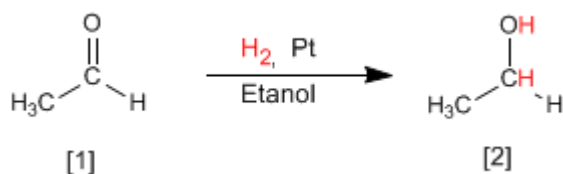
El reductor de litio y aluminio es más reactivo que el de boro, reacciona con el agua y los alcoholes desprendiendo hidrógeno. Por ello, debe disolverse en medios apróticos (éter).



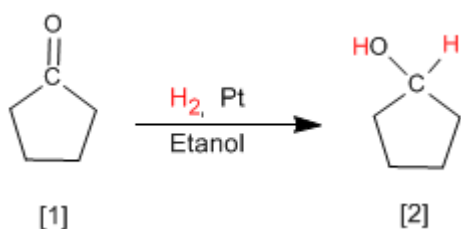
El reductor de boro, menos reactivo, descompone lentamente en medios próticos, lo que permite utilizarlo disuelto en etanol o agua.

## Síntesis de Alcoholes por hidrogenación de Carbonilos

Otro método para preparar alcoholes consiste en la reducción de aldehídos o cetonas a alcoholes. El método más simple es la hidrogenación del doble enlace carbono-oxígeno, utilizando hidrógeno en presencia de un catalizador de platino, paladio, níquel o rutenio.



El etanal [1] se transforma por hidrogenación del doble enlace en etanol [2]



La ciclopentanona [1] se transforma por hidrogenación en ciclopentanol [2]

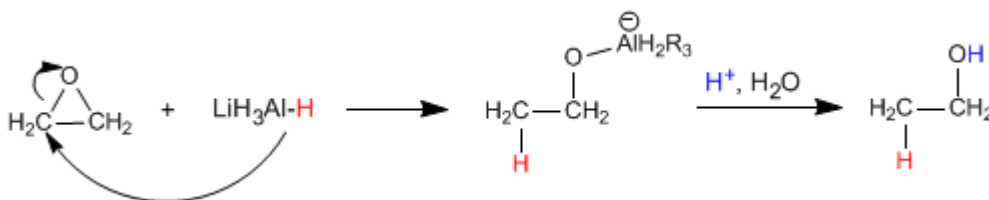
## Síntesis de Alcoholes a partir de Epóxidos

Los alcoholes se pueden obtener por apertura de epóxidos (oxaciclopropanos). Esta apertura se puede realizar empleando reactivos organometálicos o el reductor de litio y aluminio.



El oxaciclopropano [1] se transforma por reducción con hidruro de litio y aluminio en etanol [2].

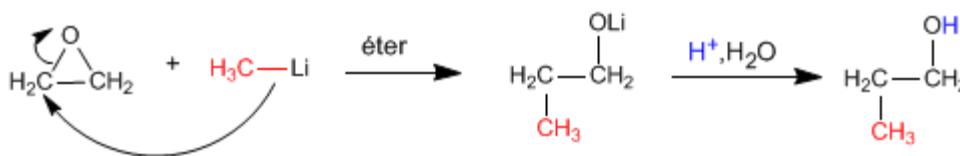
El mecanismo de la reacción comienza con el ataque del hidruro procedente del reductor sobre el carbono polarizado positivamente del epóxido, para terminar con la protonación del alcóxido.



Los reactivos de Grignard (organometálicos de magnesio) y los organolitícos reaccionan con oxaciclopropano para dar un alcohol primario.



El metillitio ataca al oxaciclopropano [1] para formar propan-1-ol [2].

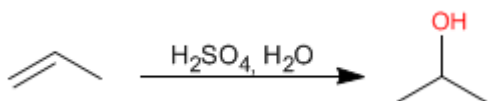


## Síntesis de Alcoholes por Hidratación de Alquenos

Un método de síntesis para alcoholes, ya estudiado en la sección de alquenos, consiste en hidratar el alqueno. La adición del -OH puede ser en el carbono más sustituido del alqueno (Markovnikov), o bien, en el carbono menos sustituido (antiMarkovnikov).

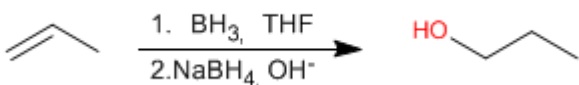
### Hidratación Markovnikov

En esta hidratación el grupo hidroxilo va al carbono con más sustituyentes. Se emplea como reactivo sulfúrico acuoso, o bien, acetato de mercurio en agua, seguido de reducción con borohidruro de sodio.



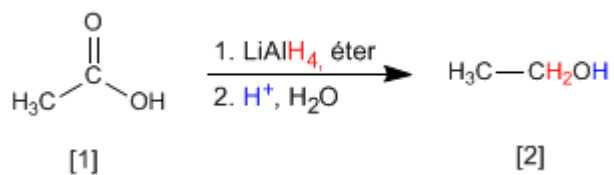
### Hidratación antiMarkovnikov

El grupo hidroxilo se adiciona al carbono menos sustituido. El reactivo empleado es borano en THF seguido de oxidación con agua oxigenada en medio básico (hidroboración)

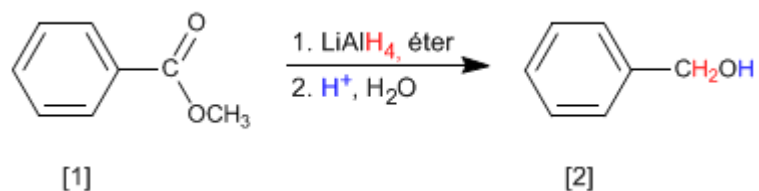


## Síntesis de alcoholes por reducción de ácidos y ésteres

Los ácidos carboxílicos y los ésteres se reducen a alcoholes con el hidruro de litio y aluminio.  
Reductores más suaves como el borohidruro de sodio son incapaces de reducir estos compuestos.



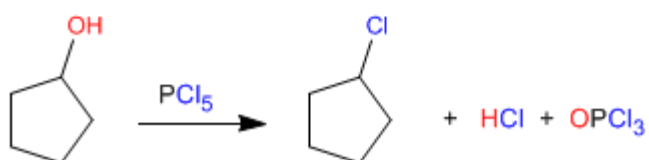
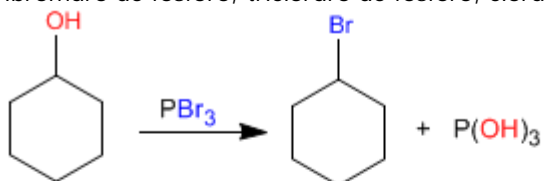
El ácido etanoico [1] se transforma por reducción con hidruro de litio y aluminio en etanol [2].



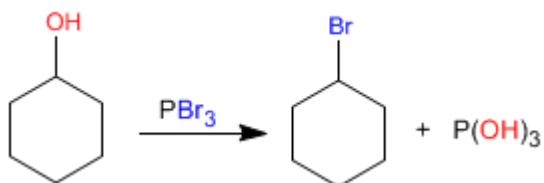
El benzoato de metilo [1] se transforma en alcohol bencílico [2] por reducción con hidruro de litio y aluminio.

## Síntesis de Haloalcanos a partir de Alcoholes

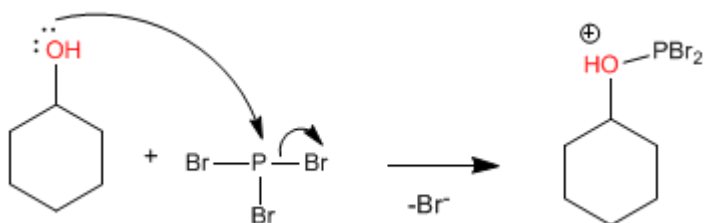
Los alcoholes primarios y secundarios pueden convertirse en haloalcanos con reactivos como: tribromuro de fósforo, tricloruro de fósforo, cloruro de tionilo y pentacloruro de fósforo.



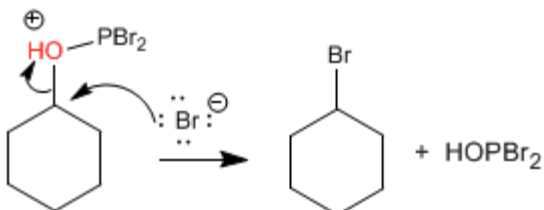
El mecanismo de estas reacciones es de tipo  $\text{S}_{\text{N}}2$  y sólo los alcoholes primarios y secundarios reaccionan. Veamos el mecanismo de la primera reacción.



**Etapas 1.** Ataque del alcohol al tribromuro de fósforo



**Etapas 2.** Sustitución nucleófila bimolecular, actuando el bromuro como nucleófilo

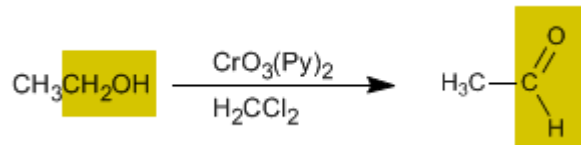


Todos los bromos del  $\text{PBr}_3$  son reactivos y el mecanismo se repite dos veces más.

## Oxidación de Alcoholes

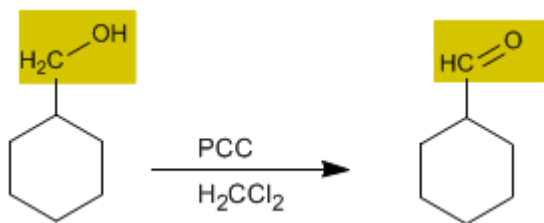
La oxidación de alcoholes forma compuestos carbonilos. Al oxidar alcoholes primarios se obtienen aldehídos, mientras que la oxidación de alcoholes secundarios forma cetonas.

### Oxidación de alcoholes primarios a aldehídos



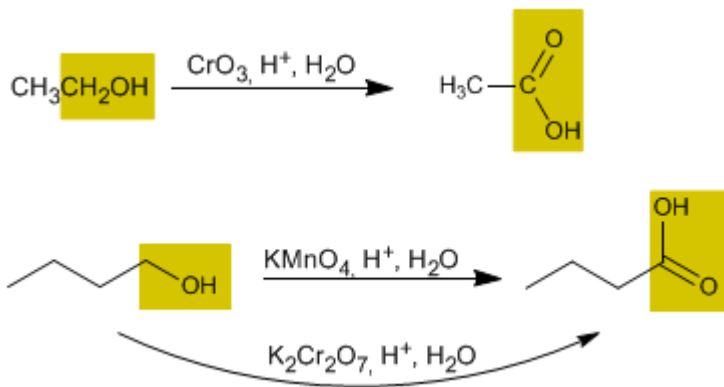
El trióxido de cromo con piridina en diclorometano permite aislar aldehídos con buen rendimiento a partir de alcoholes primarios.

Se conoce como PCC (clorocromato de piridinio) al trióxido de cromo con piridina y ácido clorhídrico en diclorometano. Este reactivo también convierte alcoholes primarios en aldehídos.



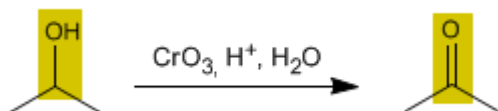
### Oxidación de alcoholes primarios a ácidos carboxílicos

El trióxido de cromo en medio ácido acuoso (reactivo de Jones), el permanganato de potasio y el dicromato de potasio oxidan los alcoholes primarios a ácidos carboxílicos.



### Oxidación de alcoholes secundarios a cetonas

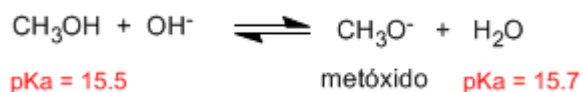
Los oxidantes convierten los alcoholes secundarios en cetonas. No es posible la sobreoxidación a ácido carboxílico.



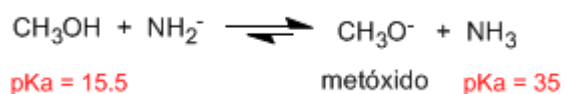


## Formación de Alcóxidos a partir de Alcoholes

Los alcóxidos son las bases de los alcoholes, se obtienen por reacción del alcohol con una base fuerte.

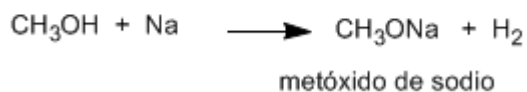
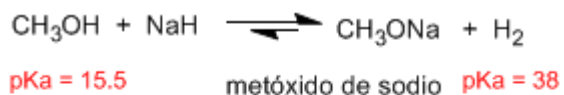


Los  $\text{pK}_a$  de los ácidos conjugados son similares y el equilibrio no se encuentra desplazado. El ión hidróxido es una base demasiado débil para formar el alcóxido en cantidad importante.



El amiduro es una base muy fuerte y desplaza el equilibrio a la derecha, transformando el metanol en metóxido.

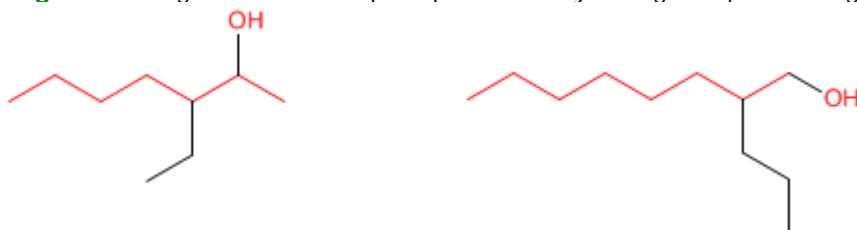
Otras bases fuertes que pueden ser usadas para formar alcóxidos son: hidruro de sodio, LDA, sodio metal.



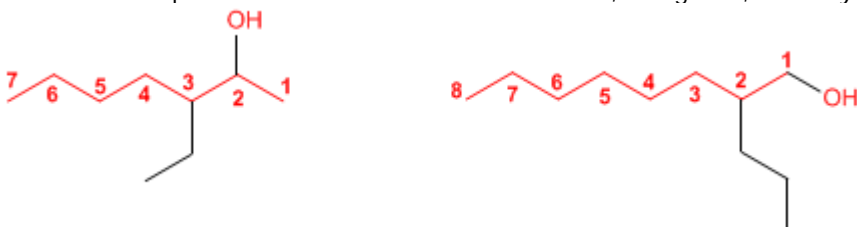
## PROBLEMAS NOMENCLATURA - ALCOHOLES

### Nomenclatura de Alcoholes - Reglas IUPAC

**Regla 1.** Se elige como cadena principal la de mayor longitud que contenga el grupo -OH.



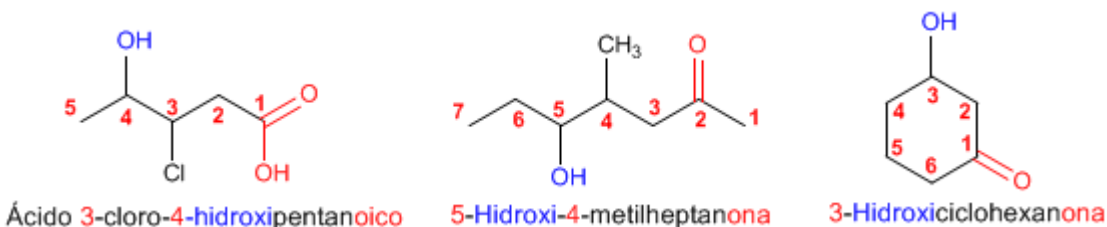
**Regla 2.** Se numera la cadena principal para que el grupo -OH tome el localizador más bajo. El grupo hidroxilo tiene preferencia sobre cadenas carbonadas, halógenos, dobles y triples enlaces.



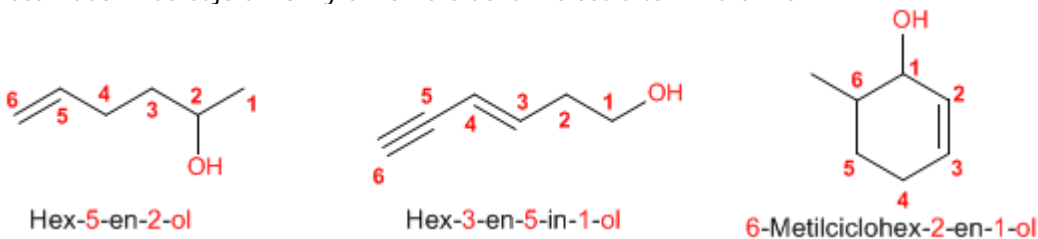
**Regla 3.** El nombre del alcohol se construye cambiando la terminación -o del alcano con igual número de carbonos por -ol



**Regla 4.** Cuando en la molécula hay grupos funcionales de mayor prioridad, el alcohol pasa a ser un mero sustituyente y se llama **hidroxi-**. Son prioritarios frente a los alcoholes: ácidos carboxílicos, anhídridos, ésteres, haluros de alcanoilo, amidas, nitrilos, aldehídos y cetonas.

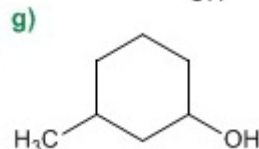
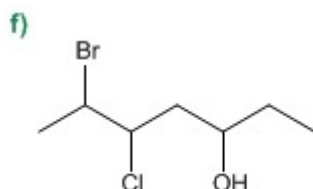
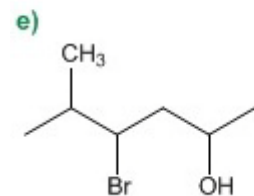
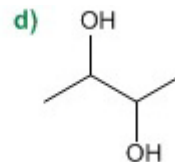
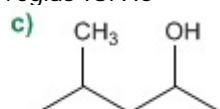
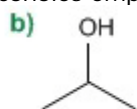
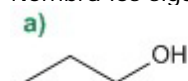


**Regla 5.** El grupo -OH es prioritario frente a los alquenos y alquinos. La numeración otorga el localizador más bajo al -OH y el nombre de la molécula termina en -ol.

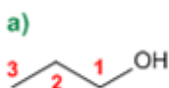


## Nomenclatura de Alcoholes - Problema 0.1

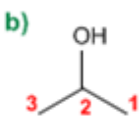
Nombra los siguientes alcoholes empleando reglas IUPAC



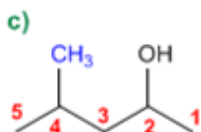
### Solución:



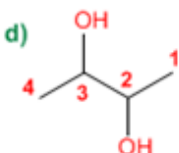
1. Cadena principal: la de mayor longitud que contenga el -OH (propano)
2. Numeración: otorga al -OH el localizador más bajo.
3. Sustituyentes: no
4. Nombre: Propan-1-ol



1. Cadena principal: la de mayor longitud que contenga el -OH (propano)
2. Numeración: indiferente.
3. Sustituyentes: no
4. Nombre: Propan-2-ol



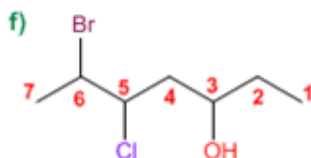
1. Cadena principal: la de mayor longitud que contenga el -OH (pentano)
2. Numeración: otorga al -OH el localizador más bajo (-OH preferente sobre cadenas)
3. Sustituyentes: metilo en 4
4. Nombre: 4-Metilpentan-2-ol



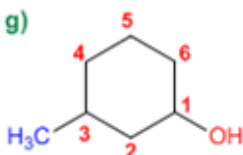
1. Cadena principal: mayor longitud (butano)
2. Numeración: comienza en uno de los extremos.
3. Sustituyentes: no
4. Nombre: Butano-2,3-diol



1. Cadena principal: mayor longitud (hexano)
2. Numeración: comienza en el extremo derecho, para otorgar al -OH el localizador más bajo.
3. Sustituyentes: bromo en posición 4 y metilo en 5.
4. Nombre: 4-Bromo-5-metilhexan-2-ol



1. Cadena principal: mayor longitud (heptano)
2. Numeración: comienza en extremo que otorga el localizador más bajo al -OH.
3. Sustituyentes: bromo en 6 y cloro en 5.
4. Nombre: 6-Bromo-5-cloroheptan-3-ol



1. Cadena principal: ciclo de seis miembros (ciclohexano)
2. Numeración: comienza en el carbono del -OH.
3. Sustituyentes: metilo en 3.
4. Nombre: 3-Metilciclohexanol

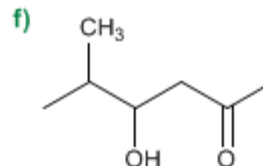
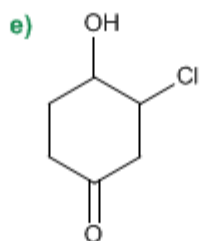
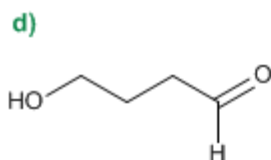
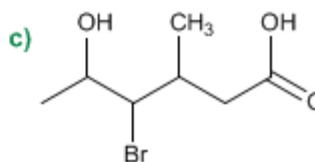
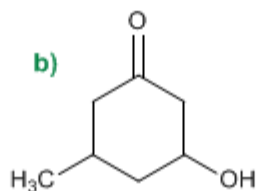
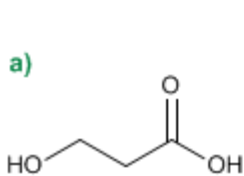
1. Cuando en una molécula hay más de un grupo -OH se pueden emplear los prefijos de cantidad di, tri, tetra, penta, hexa,..... La numeración debe otorgar los menores localizadores a los -OH.

2. El nombre del alcohol se construye comenzando por los sustituyentes, precedidos por sus respectivos localizadores, terminando en el nombre de la cadena principal. La terminación -o del alcano correspondiente se sustituye por -ol.

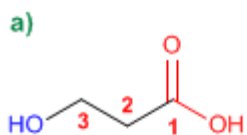
3. En el caso de alcoholes cíclicos no es necesario indicar la posición del grupo hidroxilo, puesto que siempre toma localizador 1.

## Nomenclatura de Alcoholes - Problema 0.2

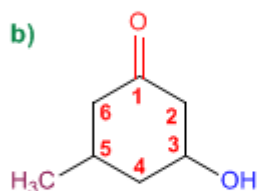
Nombra los siguientes moléculas, en las que el alcohol actúa como sustituyente.



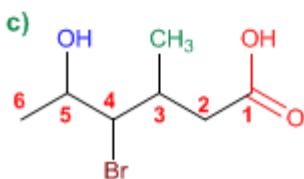
Solución



1. Cadena principal: más larga que contenga el grupo funcional (propano)
2. Grupo funcional: ácido carboxílico
3. Numeración: localizador más bajo al grupo ácido
4. Sustituyentes: grupo **hidroxi** en 3.
5. Nombre: **Acido 3-hidroxi**propanoico



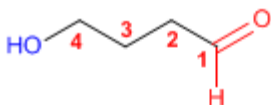
1. Cadena principal: ciclo de seis miembros (ciclohexano)
2. Grupo funcional: cetona
3. Numeración: localizador más bajo al grupo carbonilo
4. Sustituyentes: grupo **hidroxi** en 3 y **metilo** en 4.
5. Nombre: **2-Hidroxi-5-metilciclohexanona**



1. Cadena principal: más larga que contenga el grupo funcional (hexano)
2. Grupo funcional: ácido carboxílico
3. Numeración: asigna el localizador más bajo al grupo ácido.
4. Sustituyentes: **bromo** en 4, grupo **hidroxi** en 5 y **metilo** en 3
5. Nombre: **Acido 4-bromo-6-hidroxi-3-metilhexanoico**

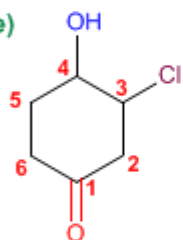
Los ácidos carboxílicos y las cetonas son prioritarios sobre los alcoholes.  
El alcohol pasa a ser un sustituyente más de la molécula, ordenándose alfabéticamente con el resto de sustituyentes.

d)



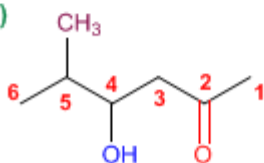
1. Cadena principal: más larga que contenga el grupo funcional (butano)
2. Grupo funcional: aldehído
3. Numeración: localizador más bajo al grupo carbonilo
4. Sustituyentes: grupo **hidroxi** en 4.
5. Nombre: **4-Hidroxibutanal**

e)



1. Cadena principal: ciclo de seis miembros
2. Grupo funcional: cetona
3. Numeración: localizador más bajo al carbonilo
4. Sustituyentes: **cloro** en 3 e **hidroxi** en 4.
5. Nombre: **3-Cloro-4-hidroxiciclohexanona**

f)



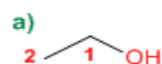
1. Cadena principal: más larga que contenga el grupo funcional (propano)
2. Grupo funcional: cetona
3. Numeración: localizador más bajo al grupo carbonilo
4. Sustituyentes: grupo **hidroxi** en 4 y **metilo** en 5.
5. Nombre: **3-Hidroxi-4-metilhexan-2-ona**

## Nomenclatura de Alcoholes - Problema 0.3

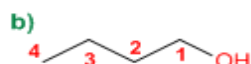
Dibujar la estructura de los siguientes alcoholes:

- |                          |                                   |
|--------------------------|-----------------------------------|
| a) Etanol                | i) Ciclopent-2-enol               |
| b) Butanol               | j) 2,3-Dimetilciclohexanol        |
| c) 2-Metilpropan-1-ol    | k) Octa-3,5-dien-2-ol             |
| d) 2-Metilbutan-2-ol     | l) Hex-4-en-1-in-3-ol             |
| e) 3-Metilbutan-2-ol     | m) 2-Bromohept-2-en-1,4-diol      |
| f) 3-Metilbutan-1-ol     | n) 2-Fenil-5-metilheptan-2-ol     |
| g) 2,3-Pentanodiol       | o) Alcohol bencílico              |
| h) 2-Etil-pent-3-en-1-ol | p) 1,2,3-Propanotriol (glicerina) |

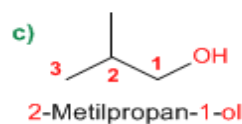
### Solución:



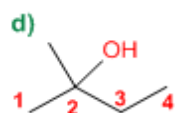
Etanol



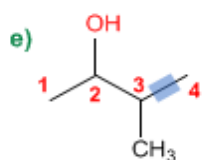
Butanol



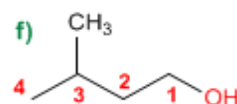
2-Metilpropan-1-ol



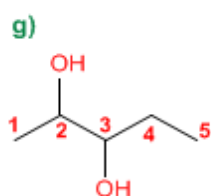
2-Metilbutan-2-ol



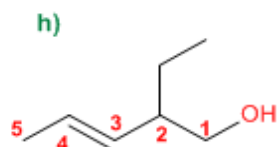
3-Metilbutan-2-ol



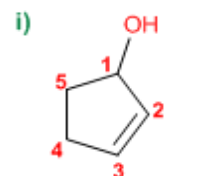
3-Metilbutan-1-ol



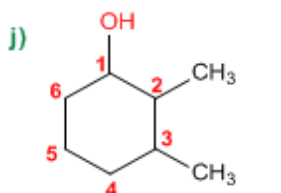
2,3-Pentanodiol



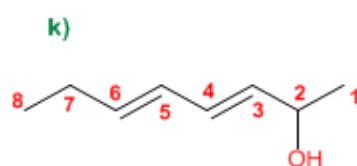
2-Etil-pent-3-en-1-ol



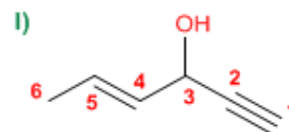
Ciclopent-2-enol



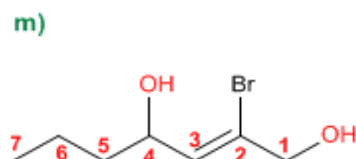
2,3-Dimetilciclohexanol



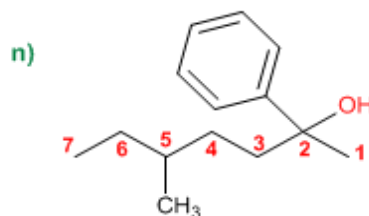
Octa-3,5-dien-2-ol



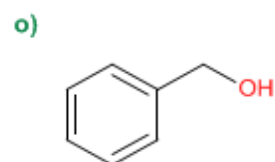
Hex-4-en-1-in-3-ol



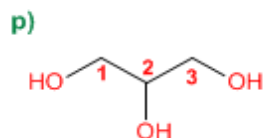
2-Bromohept-2-en-1,4-diol



2-Fenil-5-metilheptan-2-ol



Alcohol bencílico

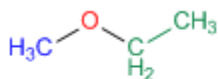


1,2,3-Propanotriol (glicerina)

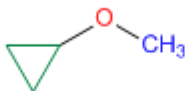
## TEORÍA DE ÉTERES

### Nomenclatura de éteres - epóxidos

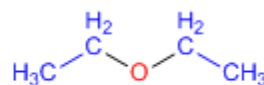
La nomenclatura de los éteres consiste en nombrar alfabéticamente los dos grupos alquilo que parten del oxígeno, terminando el nombre en éter. Veamos algunos ejemplos:



Etil metil éter

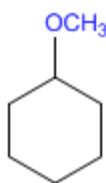


Ciclopropil metil éter

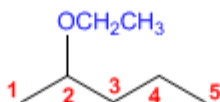


Dietil éter

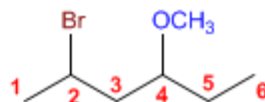
También se pueden nombrar los éteres como grupos alcoxi.



Metóxiciclohexano



2-Etoxi pentano

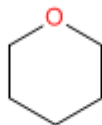


2-Bromo-4-metoxihexano

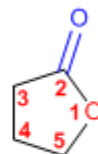
Los éteres cíclicos se forman sustituyendo  $-\text{CH}_2-$  del ciclo por  $-\text{O}-$ . Este cambio se indica con el prefijo **oxa-**.



Oxaciclopropano



Oxaciclohexano

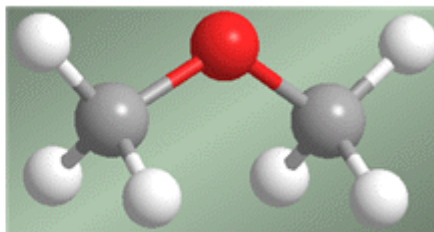
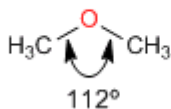
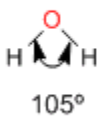


2-oxo-oxaciclopentano

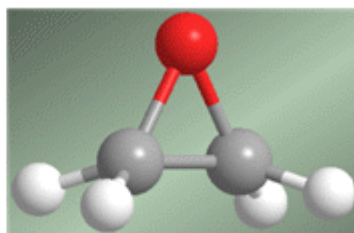
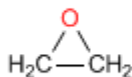


## Estructura y enlace en éteres y epóxidos

Los éteres son moléculas de estructura similar al agua y alcoholes. El ángulo entre los enlaces C-O-C es mayor que en el agua debido a las repulsiones estéricas entre grupos voluminosos.

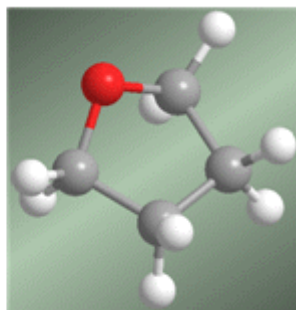
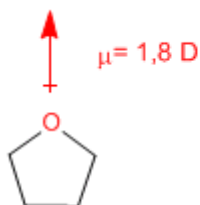


En el caso de los epóxidos la característica más relevante es la tensión del anillo, debida a ángulos de enlace muy distantes a los  $109^\circ$ .



El enlace C-O-C presenta un ángulo de  $61^\circ$ .

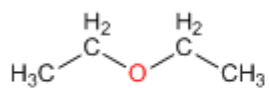
Los éteres son moléculas muy polares. Así, el Dietil éter presenta un momento dipolar de 1,2 D. Este momento dipolar es aún más importante en éteres cíclicos (oxaciclopropano, tetrahidrofurano) que presentan momentos dipolares sobre 1,8 D, similares al agua.



## Propiedades físicas de los éteres

---

Los éteres presentan unos puntos de ebullición inferiores a los alcoholes, aunque su solubilidad en agua es similar. Dada su importante estabilidad en medios básicos, se emplean como disolventes inertes en numerosas reacciones.

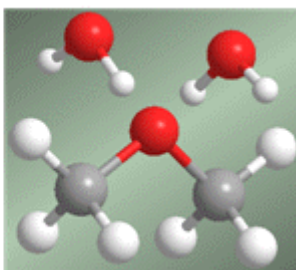
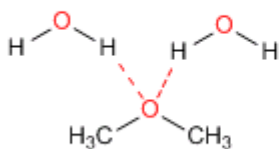


Dietil éter

P. ebul = 35°C

Solubilidad agua = 7,5 g/100ml

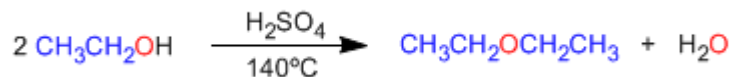
La importante solubilidad en agua se explica por los puentes de hidrógeno que se establecen entre los hidrógenos del agua y el oxígeno del éter.



## Síntesis de éteres por condensación de alcoholes

### 1. Éteres a partir de alcoholes primarios

Los éteres simétricos pueden prepararse por condensación de alcoholes. La reacción se realiza bajo calefacción (140°C) y con catálisis ácida. Así, dos moléculas de etanol condensan para formar dietil éter.

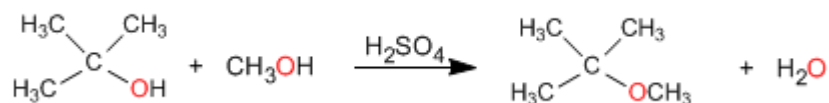


El mecanismo de la reacción transcurre en las siguientes etapas:



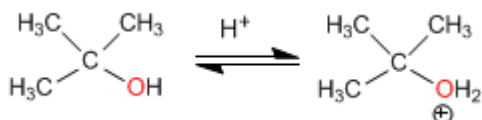
### 2. Uno de los alcoholes es secundario o terciario

En este caso la reacción transcurre en condiciones más suaves, a través de mecanismos  $\text{S}_{\text{N}}1$ .

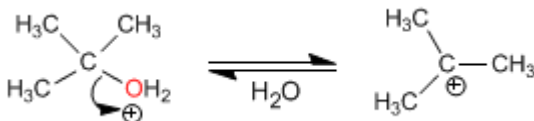


El mecanismo transcurre con formación de un carbocatión terciario de gran estabilidad

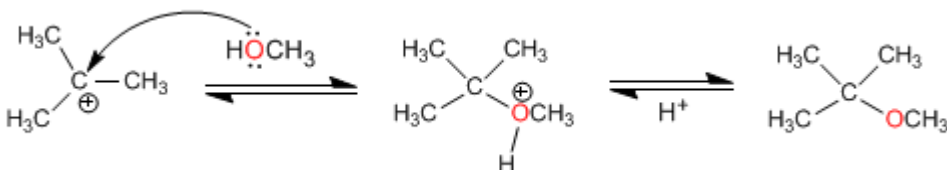
#### Etapas 1. Protonación del alcohol terciario



#### Etapas 2. Formación del carbocatión por pérdida de agua

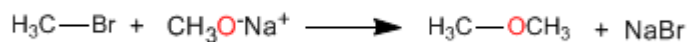


#### Etapas 3. Ataque nucleófilo del metanol



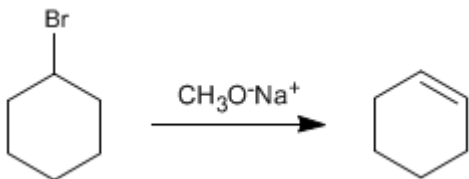
## Síntesis de Williamson de los éteres

La reacción entre un haloalcano primario y un alcóxido (o bien alcohol en medio básico) es el método más importante para preparar éteres. Esta reacción es conocida como síntesis de Williamson.

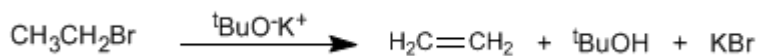


Esta reacción transcurre a través del mecanismo S<sub>N</sub>2.

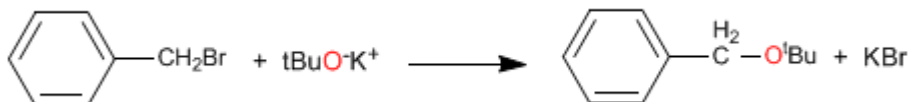
La importante basicidad de los alcóxidos produce reacciones de eliminación con sustratos secundarios y terciarios, formando alquenos en lugar de éteres.



Otra situación en la que Williamson no rinde éteres, es en el caso de emplear alcóxidos impedidos, como *tert*-butóxido de potasio. Debido a su gran tamaño el *tert*-butóxido elimina incluso con sustratos primarios.



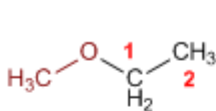
Con haloalcanos primarios y sobre todo con haloalcanos que carecen de hidrógenos β el rendimiento de Williamson es muy bueno.



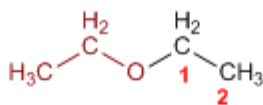
## PROBLEMAS NOMENCLATURA - ÉTERES

### Nomenclatura de Éteres - Reglas IUPAC

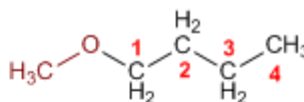
**Regla 1.** Los éteres pueden nombrarse como alcoxi derivados de alcanos (nomenclatura IUPAC sustitutiva). Se toma como cadena principal la de mayor longitud y se nombra el alcóxido como un sustituyente.



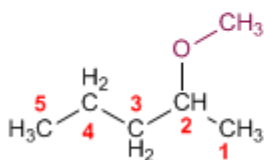
Metoxietano



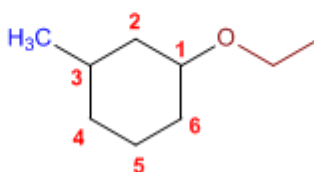
Etoxietano



1-Metoxibutano

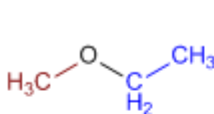


2-Metoxipentano

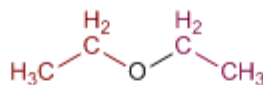


1-Etoxi-3-metilciclohexano

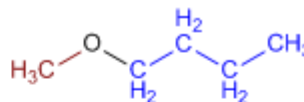
**Regla 2.** La nomenclatura funcional (IUPAC) nombra los éteres como derivados de dos grupos alquilo, ordenados alfabéticamente, terminando el nombre en la palabra éter.



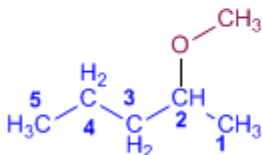
Etil metil éter



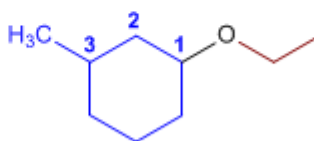
Dietil éter



Butil metil éter



Metil pent-2-il éter



Etil 3-metilciclohexil éter

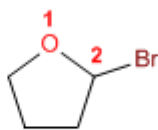
**Regla 3.** Los éteres cíclicos se forman sustituyendo un  $-\text{CH}_2-$  por  $-\text{O}-$  en un ciclo. La numeración comienza en el oxígeno y se nombran con el prefijo oxa- seguido del nombre del ciclo.



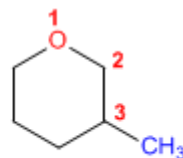
Oxaciclopropano



Oxaciclobutano



2-Bromooxaciclopentano

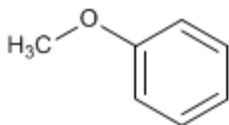


3-Metiloxaciclohexano

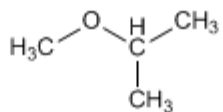
## Nomenclatura de Éteres - Problema 0.1

Nombra los siguientes éteres:

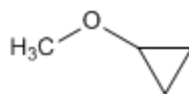
a)



b)



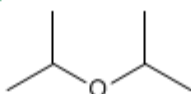
c)



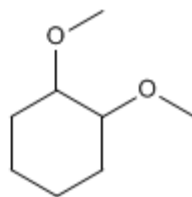
d)



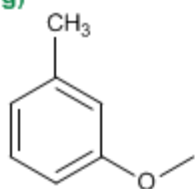
e)



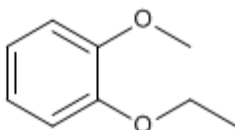
f)



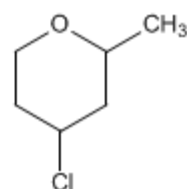
g)



h)

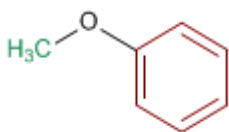


i)



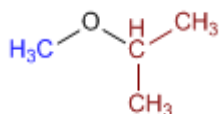
**Solución:**

a)



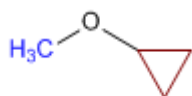
1. Sustituyentes: **fenil** y **metil**
2. Nombre: **Fenil metil** éter

b)



1. Sustituyentes: **isopropil** y **metil**
2. Nombre: **Isopropil metil** éter

c)



1. Sustituyentes: **ciclopropil** y **metil**
2. Nombre: **Ciclopropil metil** éter

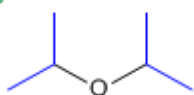
El nombre de los éteres se construye terminando en la palabra éter el nombre de las cadenas que parten del oxígeno. Estas cadenas se nombran como sustituyentes y se ordenan alfabéticamente. Obsérvese el espacio de separación entre las palabras.

d)



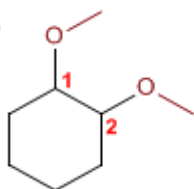
1. Sustituyentes: **etilo** y **propilo**
2. Nombre: **Etil propil** éter

e)



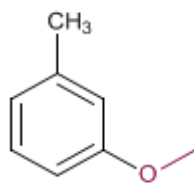
1. Sustituyentes: **isopropilos**
2. Nombre: **Diisopropil** éter

f)



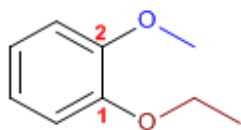
1. Cadena principal: ciclo de seis miembros (ciclohexano)
2. Numeración: otorga localizadores más bajos a sustituyentes
3. Sustituyentes: **metoxidos** en 1,2
4. Nombre: **1,2-Dimetoxiciclohexano**

g)



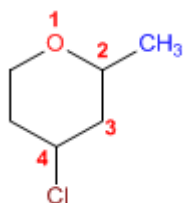
1. Cadena principal: Tolueno
2. Numeración: metilo y metóxido en meta.
3. Sustituyentes: **metoxido**
4. Nombre: **m-Metoxitolueno**

h)



1. Cadena principal: Benceno
2. Numeración: Comienza en el etoxi (antes alfabéticamente)
3. Sustituyentes: **etoxido** en 1 y **metoxido** en 2. (posición meta)
4. Nombre: **m-Etoximetoxibenceno**

i)



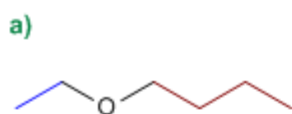
1. Cadena principal: ciclo de 6 miembros (oxaciclohexano)
2. Numeración: comienza en el oxígeno, prosigue a la derecha para otorgar a los sustituyentes los menores localizadores.
3. Sustituyentes: **cloro** y **metilo**
4. Nombre: **4-Cloro-2-metiloxaciclohexano**

## Nomenclatura de Éteres - Problema 0.2

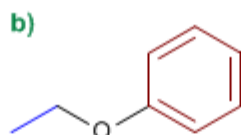
Dibuja las estructuras de los siguientes éteres:

- |                          |                                  |
|--------------------------|----------------------------------|
| a) Butil etil éter       | k) 2-Clorofenil fenil éter       |
| b) Etil fenil éter       | l) tert-butil isopropil éter     |
| c) Difenil éter          | m) 2-Metoxi-3-fenilbutan-1-ol    |
| d) Divinil éter          | n) Dietil éter                   |
| e) Isopropoxibutano      | o) m-Etoxifenol                  |
| f) Bencil fenil éter     | p) 2,3-Dimetiloxaciclopropano    |
| g) Metoxiciclohexano     | q) 3-Metoxioxaciclohexano        |
| h) 4-Metoxipent-2-eno    | r) 2-Etil-3-metiloxaciclopentano |
| i) 4-Etoxibut-1-ino      | s) Ciclohexil ciclopropil éter   |
| j) Ciclohexil fenil éter | t) 2-Metoxipentano               |

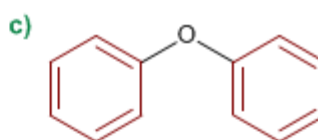
### Solución



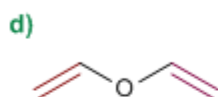
Butil etil éter



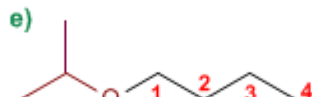
Etil fenil éter



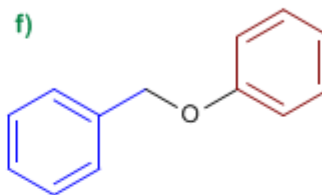
Difenil éter



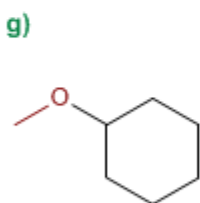
Divinil éter



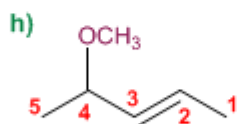
1-Isopropoxibutano



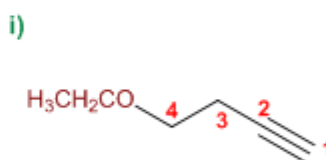
Bencil fenil éter



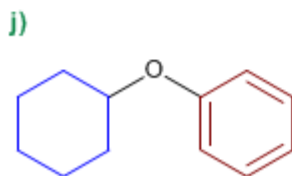
Metoxiciclohexano



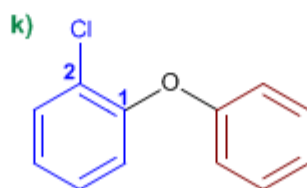
4-Metoxipent-2-eno



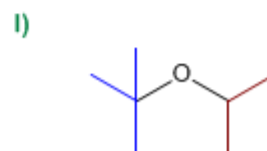
4-Etoxibut-1-ino



Ciclohexil fenil éter



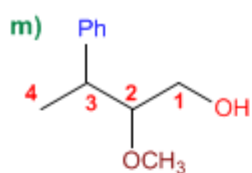
2-Clorofenil fenil éter



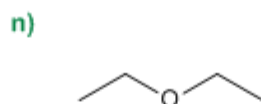
tert-butil isopropil éter



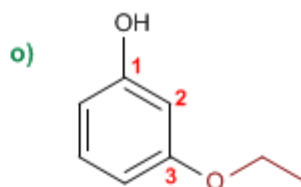
Los grupos alcóxido (metóxido, etóxido....) se ordenan alfabéticamente con los demás sustituyentes de la molécula y no tienen ninguna preferencia sobre ellos



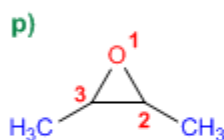
2-Metoxi-3-fenilbutan-1-ol



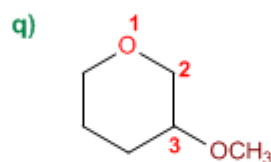
Dietil éter



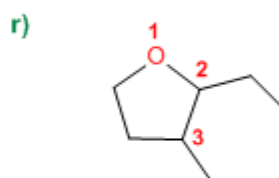
*m*-Etoxifenol



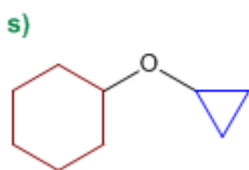
2,3-Dimetiloxaciclopropano



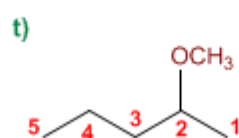
3-Metoxioxaciclohexano



2-Etil-3-metiloxaciclopentano



Ciclohexil ciclopropil éter

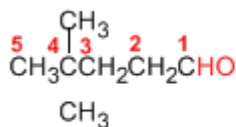


2-Metoxipentano

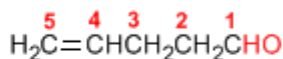
## Nomenclatura de Aldehídos y Cetonas

Los aldehídos se nombran reemplazando la terminación **-ano** del alcano correspondiente por **-al**. No es necesario especificar la posición del grupo aldehído, puesto que ocupa el extremo de la cadena (localizador 1).

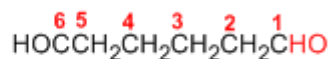
Cuando la cadena contiene dos funciones aldehído se emplea el sufijo **-dial**.



4,4-Dimetilpentanal

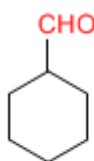


Hex-4-enal

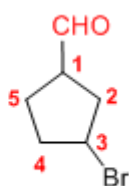


Pentanodial

El grupo **-CHO** unido a un ciclo se llama **-carbaldehído**. La numeración del ciclo se realiza dando localizador 1 al carbono del ciclo que contiene el grupo aldehído.



Ciclohexanocarbaldehído

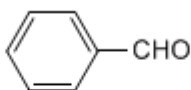


3-Bromociclopentanocarbaldehído

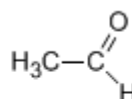
Algunos nombres comunes de aldehídos aceptados por la IUPAC son:



Formaldehído  
(Metanal)

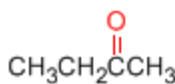


Benzaldehído  
(Bencenocarbaldehído)

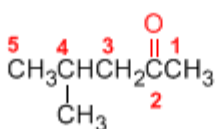


Acetaldehído  
(Etanal)

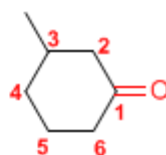
Las cetonas se nombran sustituyendo la terminación **-ano** del alcano con igual longitud de cadena por **-ona**. Se toma como cadena principal la de mayor longitud que contiene el grupo carbonilo y se numera para que éste tome el localizador más bajo.



Butanona

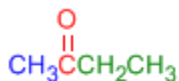


4-Metil-2-pentanona

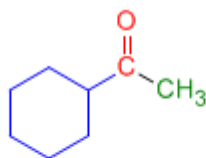


3-Metilciclohexanona

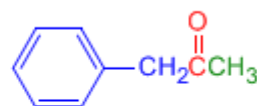
Existe un segundo tipo de nomenclatura para las cetonas, que consiste en nombrar las cadenas como sustituyentes, ordenándolas alfabéticamente y terminando el nombre con la palabra **cetona**.



Etil metil cetona



Ciclohexil metil cetona



Fenil metil cetona

[Siguiente >](#)

[\[Volver\]](#)

## Charles Friedel (1832 - 1899)



**Origen:** Químico frances..

**Lugar de nacimiento:** Estrasburgo.

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

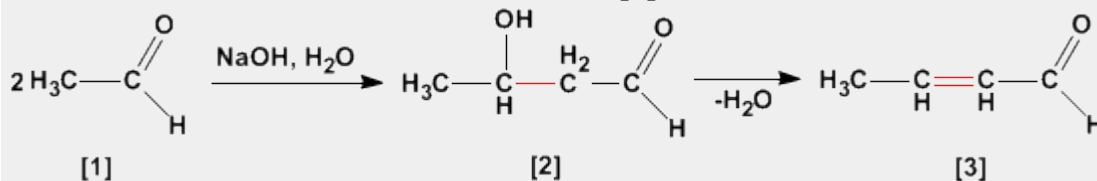
**Docencia:** Profesor en la Universidad de la Sorbona.

**Investigación:** Obtuvo el alcohol propílico. En 1877, Friedel y Crafts describieron por primera vez la reacción del benceno con un haloalcano en presencia de un ácido de Lewis. Esta reacción produce la alquilación del benceno y se conoce como alquilación de Friedl-Crafts.

**Premio Nobel:**

## Aldólica (Condensación)

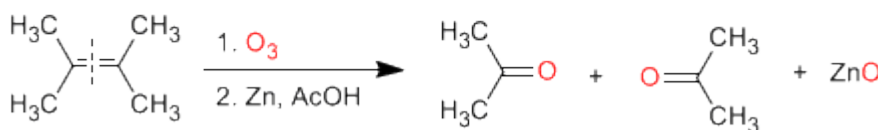
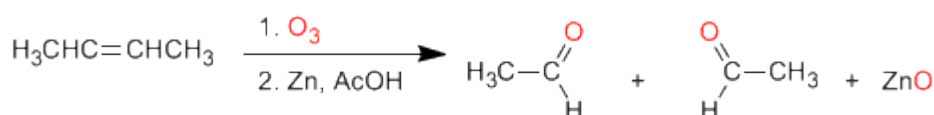
La condensación aldólica es una reacción de aldehídos o cetonas **[1]** que forma 3-hidroxicarbonilos (aldoles) **[2]**. El 3-hidroxialdehído **[2]** bajo condiciones de deshidratación por calentamiento rinde un aldehído alfa,beta-insaturado **[3]**.



## Preparación de aldehídos y cetonas

Los aldehídos y cetonas pueden ser preparados por oxidación de alcoholes, ozonólisis de alquenos, hidratación de alquinos y acilación de Friedel-Crafts como métodos de mayor importancia.

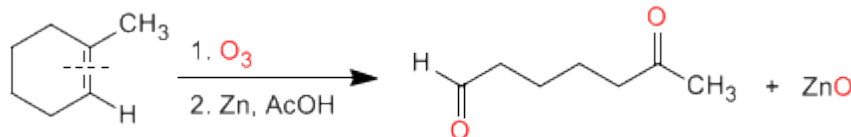
a) **Ozonólisis de alquenos:** Los alquenos rompen con ozono formando aldehídos y/o cetonas. Si el alqueno tiene hidrógenos vinílicos da aldehídos. Si tiene dos cadenas carbonadas forma cetonas.



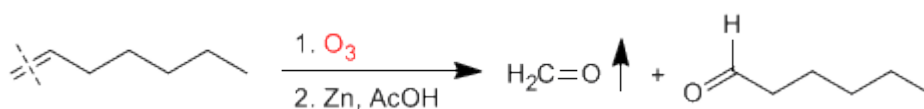
### Ozonólisis

Los alquenos simétricos y terminales permiten la preparación de carbonilos mediante ozonólisis

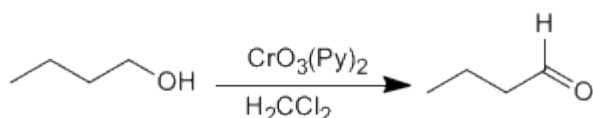
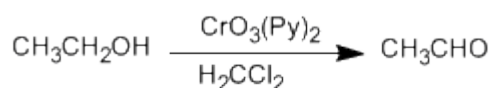
La ozonólisis de alquenos cíclicos produce compuestos dicarbonílicos:



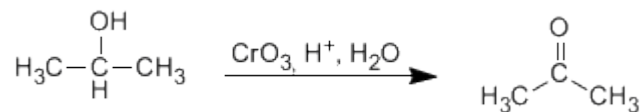
Los alquenos terminales rompen formando metanal, que separa fácilmente de la mezcla por su bajo punto de ebullición.



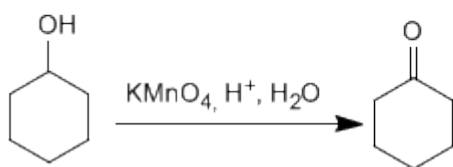
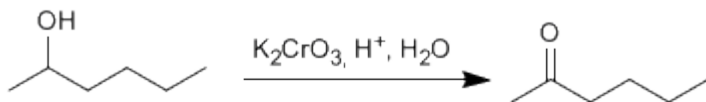
b) **Oxidación de alcoholes:** Los alcoholes primarios y secundarios se oxidan para dar aldehídos y cetonas respectivamente. Deben tomarse precauciones en la oxidación de alcoholes primarios, puesto que sobreoxidan a ácidos carboxílicos en presencia de oxidantes que contengan agua. En estos caso debe trabajarse con reactivos anhidros, como el clorocromato de piridino en diclorometano (PCC), a temperatura ambiente.



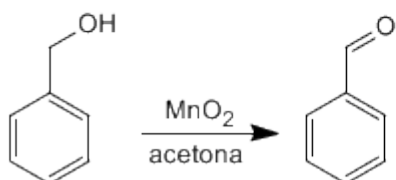
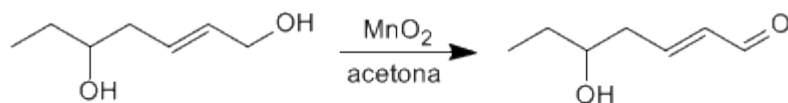
Los alcoholes secundarios dan cetonas por oxidación. Se emplean como oxidantes permanganato, dicromato, trióxido de cromo.



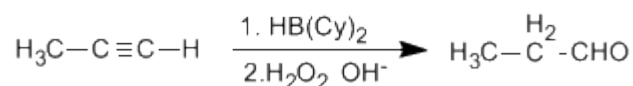
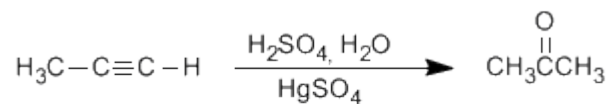
La oxidación supone la pérdida de dos hidrógenos del alcohol. Los alcoholes terciarios no pueden oxidar puesto que carecen de hidrógeno sobre el carbono.



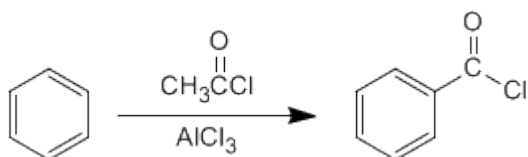
Los alcoholes alílicos y bencílicos se transforman en aldehídos o cetonas por oxidación con dióxido de manganeso en acetona. Esta reacción tiene una elevada selectividad y no oxida alcoholes que no se encuentren en dichas posiciones.



c) **Hidratación de alquinos:** Los alquinos se pueden hidratar Markovnikov, formando cetonas, o bien antiMarkovnikov, para formar aldehídos.



d) **Acilación de Friedel-Crafts:** La introducción de grupos acilo en el benceno permite la preparación de cetonas con cadenas aromáticas.



### Otto Paul Hermann Diels (1876 - 1954)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

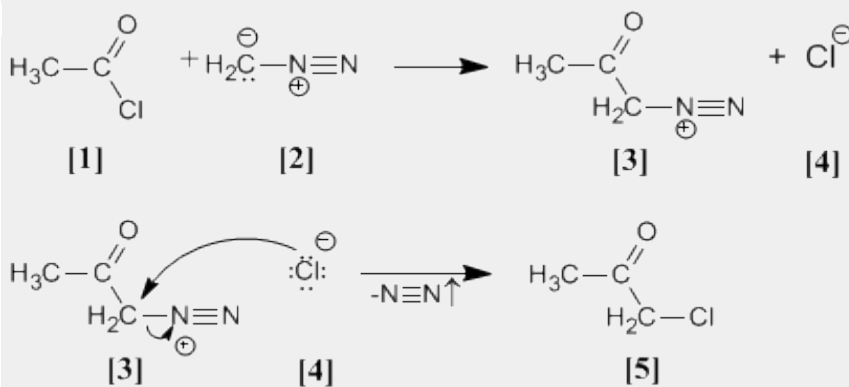
**Docencia:** profesor y jefe del departamento de química en la Universidad de Berlín. En 1916, tomó el puesto de profesor de Química en la Universidad de Kiel, cargo que no dejó hasta su jubilación en 1945.

**Investigación:** En 1906 descubrió el anhídrido malónico. Investigó en reacciones de deshidrogenación con selenio. Síntesis de  $\alpha$ -dicetonas. Pero su trabajo más importante es la reacción de Diels - Alder.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Kurt Alder

### Arndt Eistert (Síntesis)

Cloruro de acetilo [1] se trata con diazometano [2] rindiendo la sal de diazonio [3]. El cloruro [4] producido reacciona con la sal de diazonio para dar la  $\alpha$ -clorocetona [5].

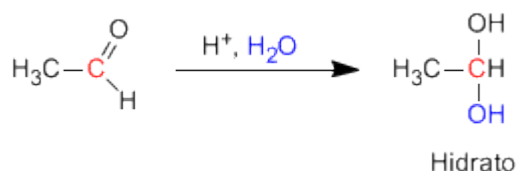


#### Síntesis de Arndt Eistert

Esta reacción permite transformar haluros de alcanoilo en cetonas halogenadas en su posición alfa.

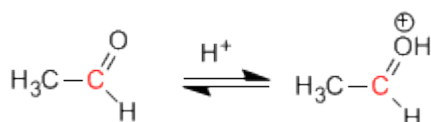
## Formación de Hidratos

Los aldehídos y cetonas reaccionan en medio ácido acuoso para formar hidratos. El mecanismo consta de tres etapas. La primera y más rápida consiste en la protonación del oxígeno carbonílico. Esta protonación produce un aumento de la polaridad sobre el carbono y favorece el ataque del nucleófilo. En la segunda etapa el agua ataca al carbono carbonilo, es la etapa lenta del mecanismo. En la tercera etapa se produce la desprotonación del oxígeno formándose el hidrato final.

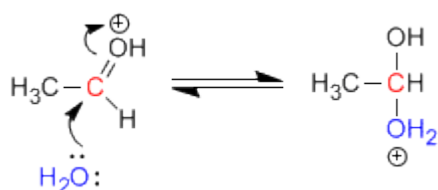


### Mecanismo de la reacción

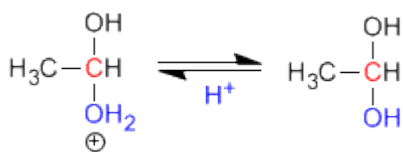
Etapa 1. Protonación del oxígeno carbonílico.



Etapa 2. Ataque nucleófilo del agua al carbonilo protonado.



Etapa 3. Desprotonación del hidrato





**Origen:** Químico estadounidense.

**Lugar de nacimiento:** Budapest

**Formación:** Se doctoró en la Universidad de Budapest en 1949

**Docencia:** Trabajó en el departamento de química orgánica de la Academia de Ciencias de Hungría y posteriormente en la Universidad de Cleveland.

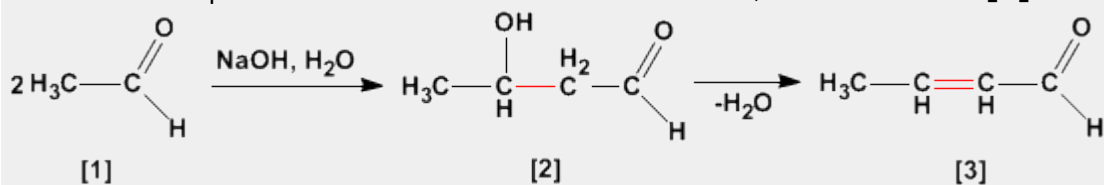
**Industria:** Trabajó en los laboratorios de la Dow Chemical de Ontario

**Investigación:** Olah consiguió preparar carbocationes estables utilizando componentes extremadamente ácidos.

**Premio Nobel:** En 1994 obtuvo el premio Nobel de Química por sus investigaciones sobre los carbocationes

### Aldólica (Condensación)

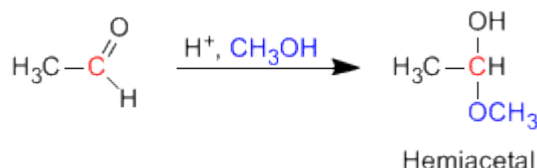
La condensación aldólica es una reacción de aldehídos o cetonas **[1]** que forma 3-hidroxicarbonilos (aldoles) **[2]**. El 3-hidroxialdehído **[2]** bajo condiciones de deshidratación por calentamiento rinde un aldehído alfa,beta-insaturado **[3]**.





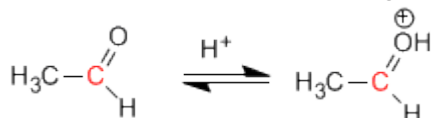
## Formación de Hemiacetales

Los hemiacetales se forman por reacción de un equivalente de alcohol con el grupo carbonilo de un aldehído o cetona. Esta reacción se cataliza con ácido y es equivalente a la formación de hidratos.

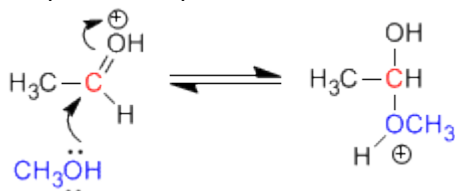


### Mecanismo de la reacción:

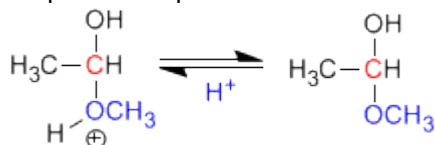
Etapas 1. Protonación del oxígeno carbonílico.



Etapas 2. Ataque nucleófilo del metanol al carbonilo protonado.



Etapas 3. Desprotonación del hemiacetal



## Otto Paul Hermann Diels (1876 - 1954)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

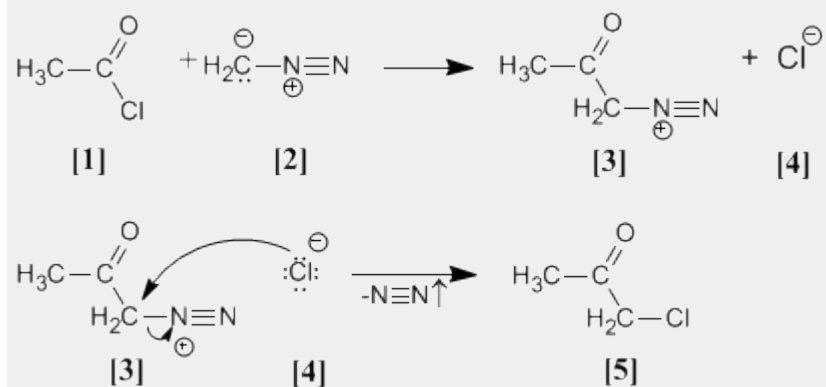
**Docencia:** profesor y jefe del departamento de química en la Universidad de Berlín. En 1916, tomó el puesto de profesor de Química en la Universidad de Kiel, cargo que no dejó hasta su jubilación en 1945.

**Investigación:** En 1906 descubrió el anhídrido malónico. Investigó en reacciones de deshidrogenación con selenio. Síntesis de  $\alpha$ -dicetonas. Pero su trabajo más importante es la reacción de Diels - Alder.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Kurt Alder

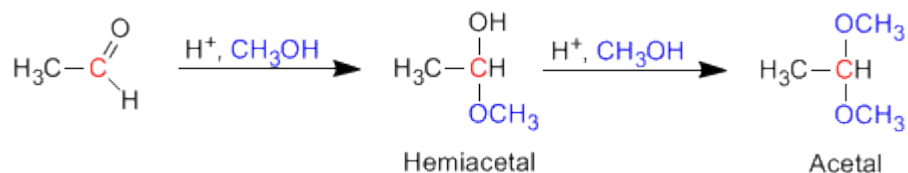
### Arndt Eistert (Síntesis)

Cloruro de acetilo **[1]** se trata con diazometano **[2]** rindiendo la sal de diazonio **[3]**. El cloruro **[4]** producido reacciona con la sal de diazonio para dar la  $\alpha$ -clorocetona **[5]**.



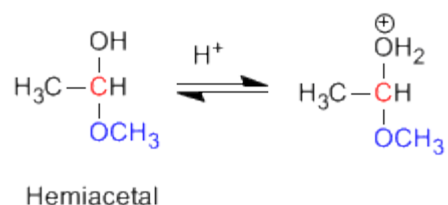
## Formación de Acetales

Los aldehídos y cetonas reaccionan con alcoholes bajo condiciones de catálisis ácida, formando en una primera etapa hemiacetales, que posteriormene evolucionan por reacción con un segundo equivalente de alcohol a acetales.

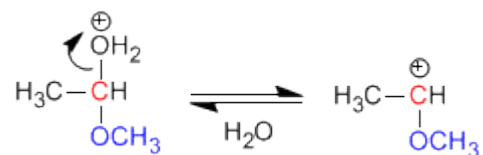


### Mecanismo para la formación de acetales

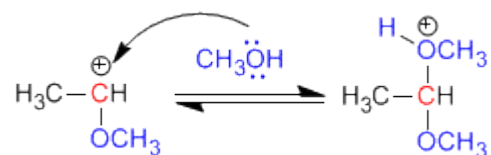
Etapa 1. Protonación del grupo hidroxilo



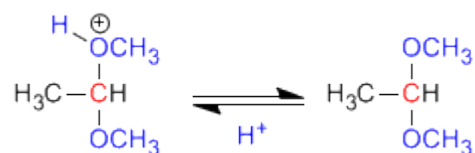
Etapa 2. Pérdida de agua.



Etapa 3. Ataque del alcohol al carbocatión



Etapa 4. Desprotonación del acetal



### Otto Paul Hermann Diels (1876 - 1954)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

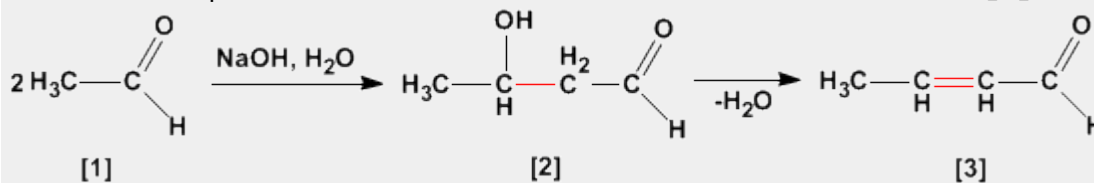
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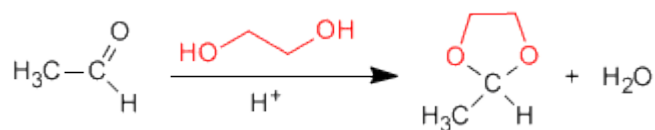
### Aldólica (Condensación)

La condensación aldólica es una reacción de aldehídos o cetonas **[1]** que forma 3-hidroxicarbonilos (aldoles) **[2]**. El 3-hidroxialdehído **[2]** bajo condiciones de deshidratación por calentamiento rinde un aldehído alfa,beta-insaturado **[3]**.



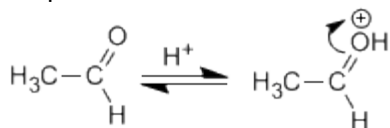
## Formación de acetales cíclicos

Los 1,2- y 1,3-dioles reaccionan con aldehídos y cetonas formando acetales cíclicos. Los equilibrios se desplazan hacia el producto final eliminando el agua formada por destilación azeotrópica con benceno o tolueno.

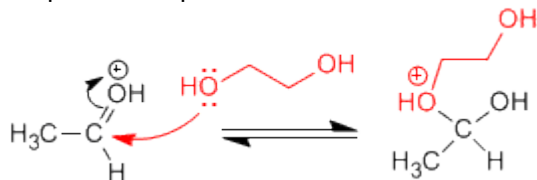


### Mecanismo para la formación de acetales cíclicos:

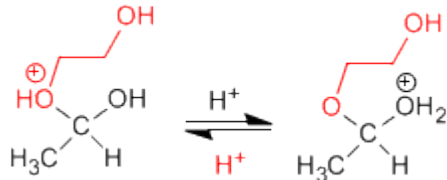
Etapa 1. Protonación del carbonilo



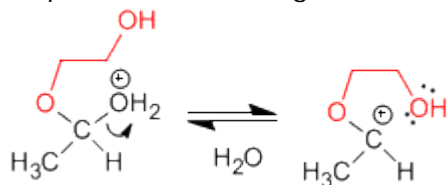
Etapa 2. Ataque nucleófilo del diol al carbonilo.



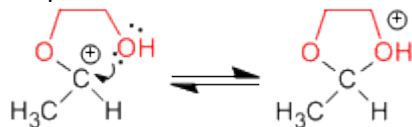
Etapa 3. Equilibrio ácido base entre el éter y el alcohol



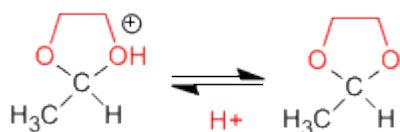
Etapa 4. Pérdida de agua



Etapa 5. Ciclación



Etapa 6. Desprotonación del acetal cíclico



### Kurt Alder (1902 - 1958)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió en la Universidad de Kiel. Bajo la supervisión del químico alemán Otto Diels, su jefe e instructor en Kiel.

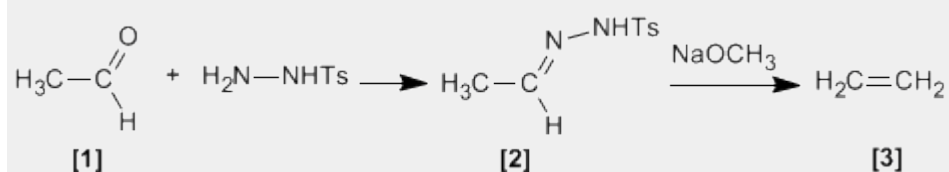
**Docencia:** Alder ejerció como profesor de química en las universidades de Kiel y Colonia.

**Investigación:** Alder se especializó en la síntesis diénica (conocida más tarde como la reacción Diels - Alder) que consiste fundamentalmente en el análisis y formación de compuestos orgánicos complejos. Ya en 1928 ambos fueron coautores de un ensayo sobre este proceso.

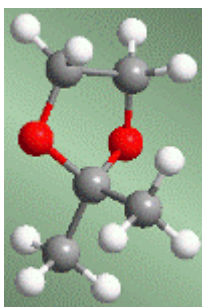
**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Diels

### Bamford Stevens (Reacción)

Tosilhidrazonas [2] de aldehídos o cetonas alifáticos [1] reaccionan con bases fuertes para dar alquenos [3].

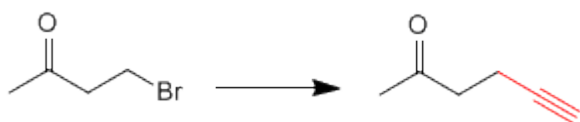


## Acetales como grupos protectores

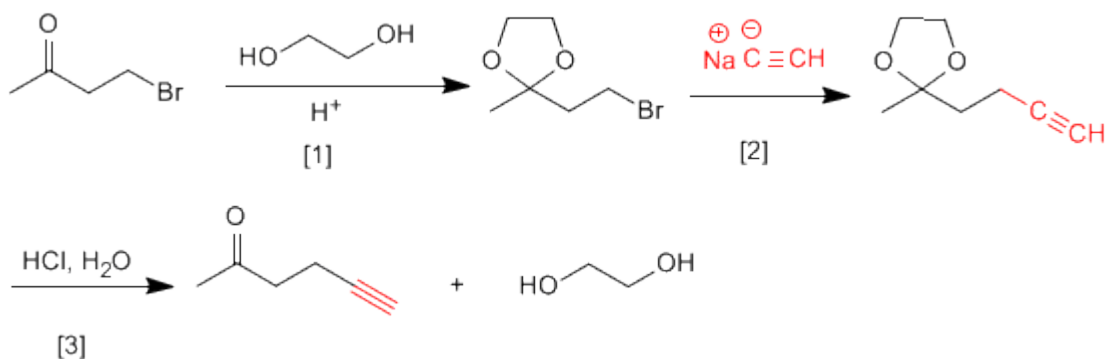


Los acetales pueden emplearse, por su estabilidad, como grupos protectores del carbonilo. El acetal es un éter, muy estable en medios básicos, aunque rompe en presencia de medios ácidos. En muchos procesos de síntesis el grupo carbonilo es incompatible con el reactivo utilizado. En estos casos debe protegerse para evitar que reaccione. La inestabilidad del acetal en medio ácido puede emplearse para desproteger el carbonilo.

Veamos algunos ejemplos:



Esta transformación requiere una sustitución, empleando como nucleófilo un acetiluro de sodio. El nucleófilo puede atacar también al grupo carbonilo, para evitarlo vamos a protegerlo.

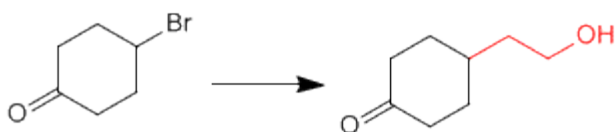


[1] Protección de la cetona.

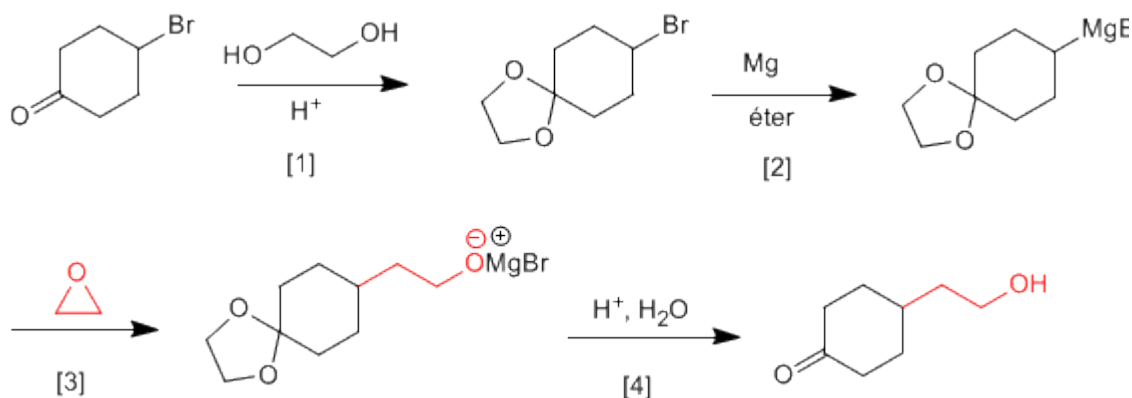
[2] Ataque del acetiluro al carbono del bromo.

[3] Desprotección del carbonilo

Veamos un segundo ejemplo:



Es necesario proteger la cetona antes de formar el organometálico para evitar la dimerización del compuesto.



- [1] Protección de la cetona.  
 [2] Formación del magnesiano.  
 [3] Apertura del oxaciclopropano.  
 [4] Desprotección y protonación del alcóxido.

### Otto Paul Hermann Diels (1876 - 1954)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

**Docencia:** profesor y jefe del departamento de química en la Universidad de Berlín. En 1916, tomó el puesto de profesor de Química en la Universidad de Kiel, cargo que no dejó hasta su jubilación en 1945.

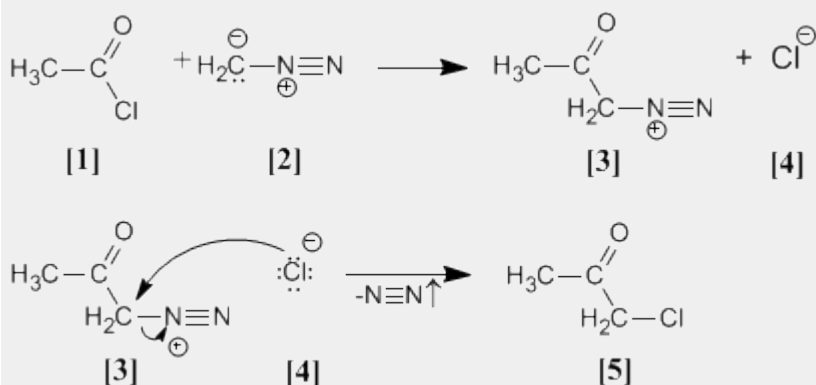
**Investigación:** En 1906 descubrió el anhídrido malónico.

Investigó en reacciones de deshidrogenación con selenio. Síntesis de  $\alpha$ -dicetonas. Pero su trabajo más importante es la reacción de Diels - Alder.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Kurt Alder

### Arndt Eistert (Síntesis)

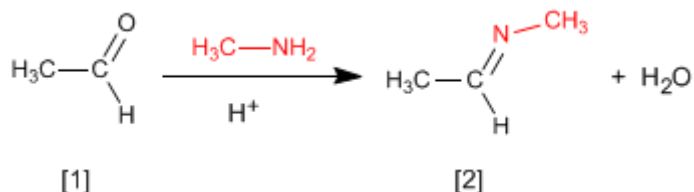
Cloruro de acetilo **[1]** se trata con diazometano **[2]** rindiendo la sal de diazonio **[3]**. El cloruro **[4]** producido reacciona con la sal de diazonio para dar la  $\alpha$ -clorocetona **[5]**.





## Formación de Iminas

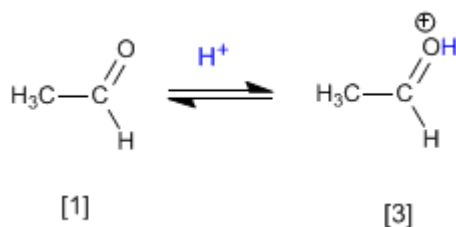
La reacción de aldehídos o cetonas **[1]** con aminas primarias genera iminas **[2]**. La reacción se favorece en un medio ligeramente ácido (pH=4.5).



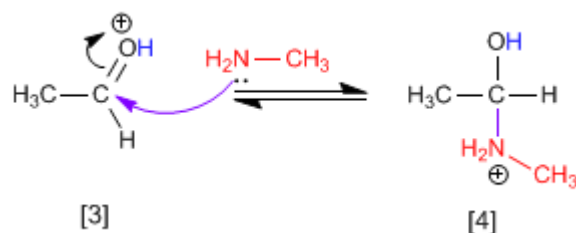
El control del pH es fundamental, puesto que se requiere la protonación del oxígeno del carbonilo para favorecer el ataque nucleófilo.

### Mecanismo:

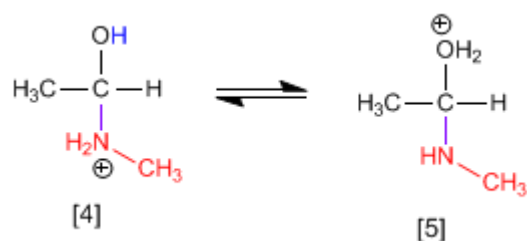
**Etapla 1.** Protonación del grupo carbonilo que aumenta la polaridad positiva sobre el carbono y favorece el ataque nucleófilo.



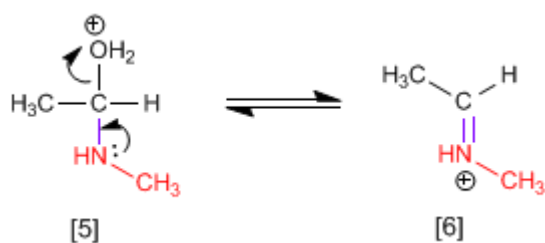
**Etapla 2.** Ataque nucleófilo de la amina primaria al carbono carbonilo.



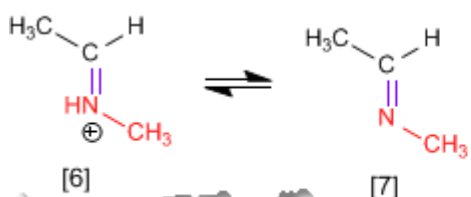
**Etapla 3.** Protonación del grupo hidroxilo para transformarlo en buen grupo saliente.



**Etapla 4.** Pérdida de agua y formación de la imina protonada.



### Etapa 5. Desprotonación del catión.



### George A. Olah (1927 - )



**Origen:** Químico estadounidense.

**Lugar de nacimiento:** Budapest

**Formación:** Se doctoró en la Universidad de Budapest en 1949

**Docencia:** Trabajó en el departamento de química orgánica de la Academia de Ciencias de Hungría y posteriormente en la Universidad de Cleveland.

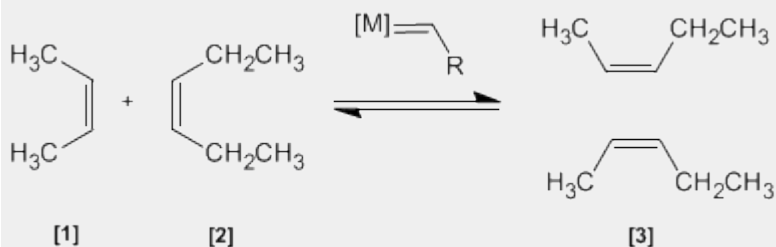
**Industria:** Trabajó en los laboratorios de la Dow Chemical de Ontario

**Investigación:** Olah consiguió preparar carbocationes estables utilizando componentes extremadamente ácidos.

**Premio Nobel:** En 1994 obtuvo el premio Nobel de Química por sus investigaciones sobre los carbocationes

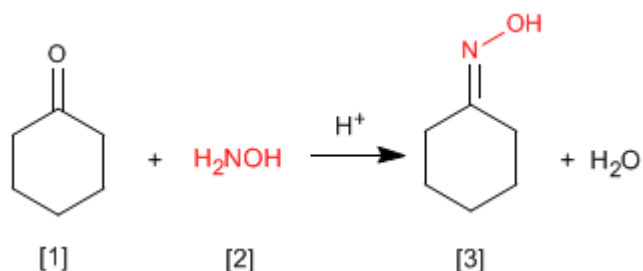
### Metátesis de Alquenos

En esta reacción dos alquenos **[1]** y **[2]** son tratados con un metal de transición que actúa como catalizador, dando una mezcla de alquenos **[3]** (incluyendo isómeros Z/E). Este productos se obtiene por intercambio de grupos alquilideno.

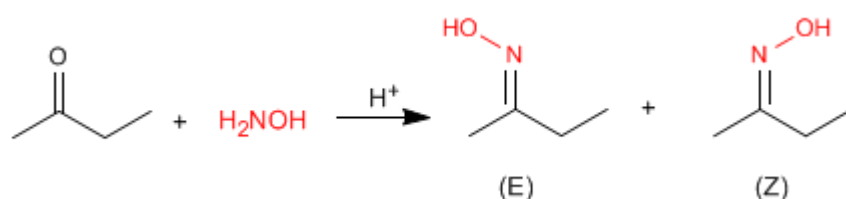


## Formación de Oximas

Las oximas [3] se obtienen por reacción de aldehídos o cetonas [1] e hidroxilamina [2] en un medio débilmente ácido. El mecanismo es análogo al de formación de iminas.



Las oximas de aldehídos y cetona asimétricas presentan isomería Z/E dependiendo de la posición del hidroxilo.



Las iminas e hidrazonas (que comentaremos a continuación) también presentan esta característica.

### George A. Olah (1927 - )



**Origen:** Químico estadounidense.

**Lugar de nacimiento:** Budapest

**Formación:** Se doctoró en la Universidad de Budapest en 1949

**Docencia:** Trabajó en el departamento de química orgánica de la Academia de Ciencias de Hungría y posteriormente en la Universidad de Cleveland.

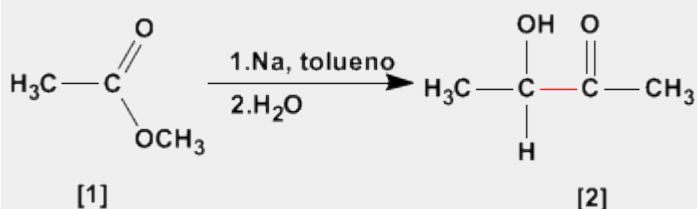
**Industria:** Trabajó en los laboratorios de la Dow Chemical de Ontario

**Investigación:** Olah consiguió preparar carbocationes estables utilizando componentes extremadamente ácidos.

**Premio Nobel:** En 1994 obtuvo el premio Nobel de Química por sus investigaciones sobre los carbocationes

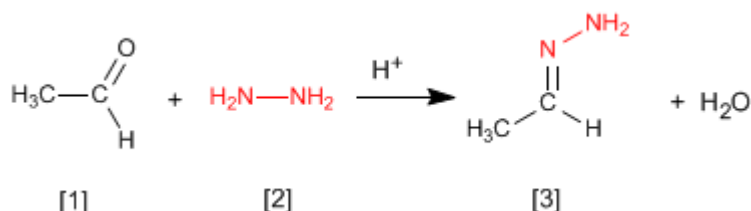
## Aciloinica (Condensación)

La condensación aciloinica transforma ésteres [1] en alfa-hidroxicetonas [2]. Esta reacción se realiza con sodio metal en disolvente inerte.

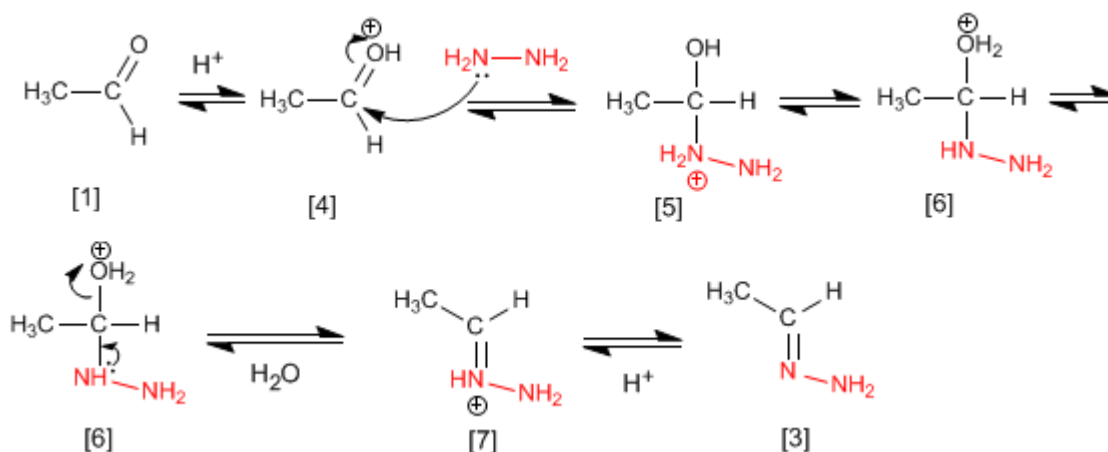


## Formación de Hidrazonas

Las hidrazonas **[3]** se obtienen por reacción de aldehídos o cetonas **[1]** con hidrazina **[2]**. Igual que en el caso de las iminas y oximas requiere pH=4.



Aunque el mecanismo es análogo al de formación de iminas, comentaremos de nuevo los pasos.



El etanal **[1]** se protona formando su ácido conjugado **[4]**. La importante polaridad del carbono carbonilo de **[4]** favorece el ataque de la hidrazina **[2]** para formando el intermedio **[5]**. El compuesto **[5]** intercambia un protón entre el nitrógeno y el oxígeno, transformando el grupo hidroxilo en agua (buen grupo saliente). El intermedio **[6]** pierde una molécula de agua transformándose en **[7]**, cuya desprotonación da la hidrazona final **[3]**.

### Kurt Alder (1902 - 1958)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió en la Universidad de Kiel. Bajo la supervisión del químico alemán Otto Diels, su jefe e instructor en Kiel.

**Docencia:** Alder ejerció como profesor de química en las universidades de Kiel y Colonia.

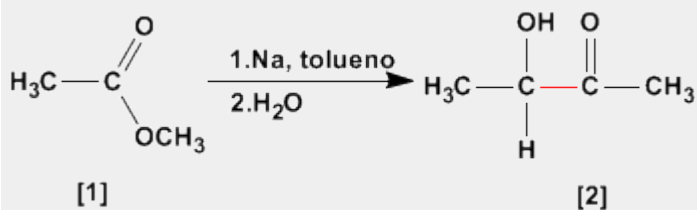
**Investigación:** Alder se especializó en la síntesis diénica (conocida más tarde como la reacción Diels - Alder) que consiste fundamentalmente en el análisis y formación de compuestos orgánicos complejos.

Ya en 1928 ambos fueron coautores de un ensayo sobre este proceso.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Diels

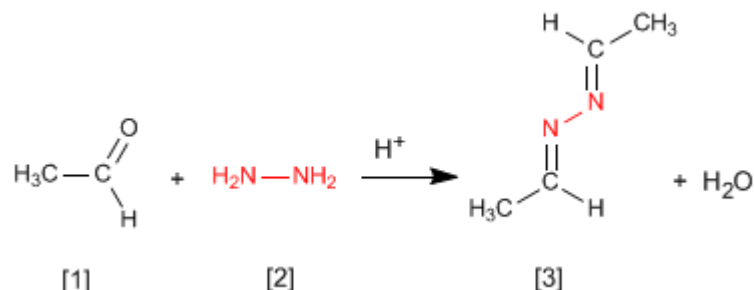
### Aciloínica (Condensación)

La condensación aciloínica transforma esteres [1] en alfa-hidroxicetonas [2]. Esta reacción se realiza con sodio metal en disolvente inerte.



## Formación de Azinas

La hidrazina [2] reacciona con dos moléculas de aldehído [1] para formar azinas [3].



El mecanismo es análogo al de formación de iminas, oximas e hidrazonas.

### George A. Olah (1927 - )



**Origen:** Químico estadounidense.

**Lugar de nacimiento:** Budapest

**Formación:** Se doctoró en la Universidad de Budapest en 1949

**Docencia:** Trabajó en el departamento de química orgánica de la Academia de Ciencias de Hungría y posteriormente en la

Universidad de Cleveland.

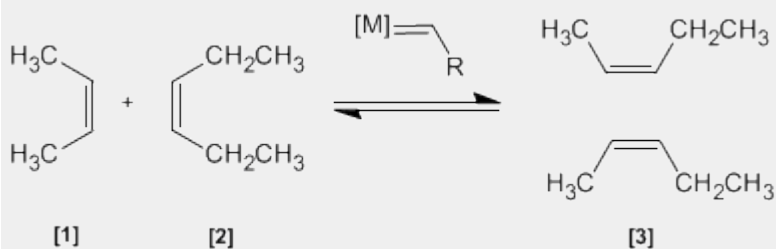
**Industria:** Trabajó en los laboratorios de la Dow Chemical de Ontario

**Investigación:** Olah consiguió preparar carbocationes estables utilizando componentes extremadamente ácidos.

**Premio Nobel:** En 1994 obtuvo el premio Nobel de Química por sus investigaciones sobre los carbocationes

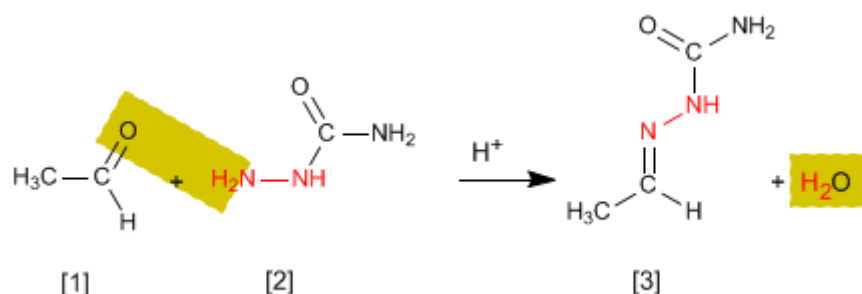
## Metátesis de Alquenos

En esta reacción dos alquenos [1] y [2] son tratados con un metal de transición que actúa como catalizador, dando una mezcla de alquenos [3] (incluyendo isómeros Z/E). Este producto se obtiene por intercambio de grupos alquilideno.



## Formación de Semicarbazonas

Las semicarbazonas [3] se obtienen por reacción de aldehídos o cetonas [1] con semicarbazida [2]. Veamos un ejemplo:



El mecanismo es análogo al de formación de iminas, oximas e hidrazonas.

### Charles Friedel (1832 - 1899)



**Origen:** Químico frances..

**Lugar de nacimiento:** Estrasburgo.

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

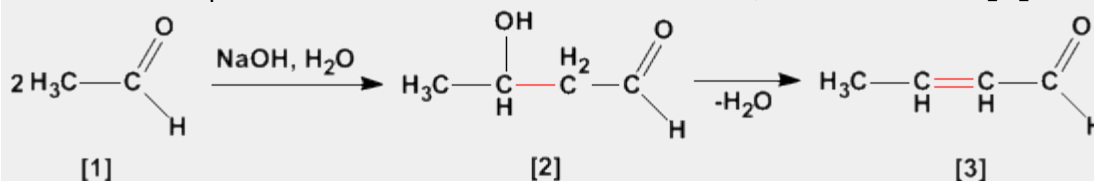
**Docencia:** Profesor en la Universidad de la Sorbona.

**Investigación:** Obtuvo el alcohol propílico. En 1877, Friedel y Crafts describieron por primera vez la reacción del benceno con un haloalcano en presencia de un ácido de Lewis. Esta reacción produce la alquilación del benceno y se conoce como alquilación de Friedl-Crafts.

**Premio Nobel:**

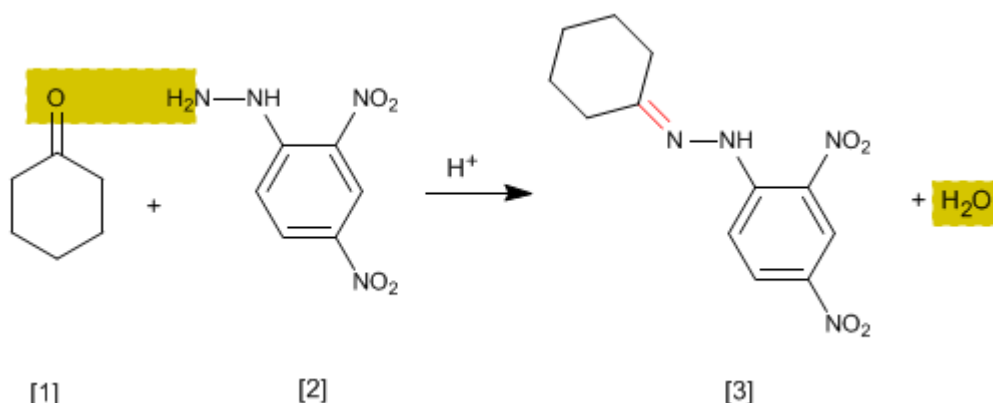
### Aldólica (Condensación)

La condensación aldólica es una reacción de aldehídos o cetonas [1] que forma 3-hidroxicarbonilos (aldoles) [2]. El 3-hidroxiacetaldehído [2] bajo condiciones de deshidratación por calentamiento rinde un aldehído alfa,beta-insaturado [3].



## Ensayo de la 2,4-Dinitrofenilhidrazina

Se trata de un ensayo analítico específico de aldehídos y cetonas. Los carbonilos **[1]** reaccionan con 2,4-Dinitrofenilhidrazina **[2]** formando fenilhidrazonas **[3]** que precipitan de color amarillo. La aparición de precipitado es un indicador de la presencia de carbonilos en el medio.



El mecanismo de la reacción es análogo al de formación de iminas.

### Kurt Alder (1902 - 1958)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió en la Universidad de Kiel. Bajo la supervisión del químico alemán Otto Diels, su jefe e instructor en Kiel.

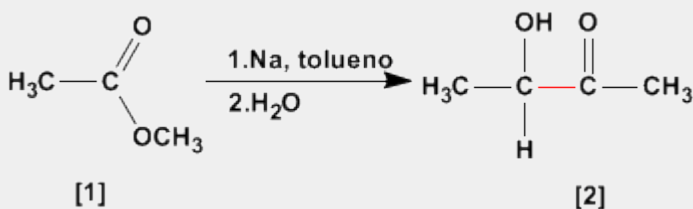
**Docencia:** Alder ejerció como profesor de química en las universidades de Kiel y Colonia.

**Investigación:** Alder se especializó en la síntesis diénica (conocida más tarde como la reacción Diels - Alder) que consiste fundamentalmente en el análisis y formación de compuestos orgánicos complejos. Ya en 1928 ambos fueron coautores de un ensayo sobre este proceso.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Diels

### Aciloinica (Condensación)

La condensación aciloinica transforma esteres **[1]** en alfa-hidroxicetonas **[2]**. Esta reacción se realiza con sodio metal en disolvente inerte.





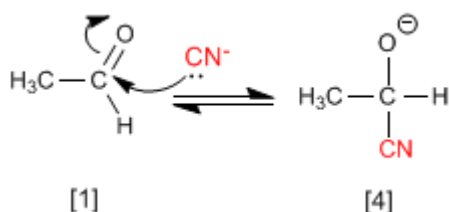
## Formación de Cianhidrinas

Las cianhidrinas **[3]** se forman por reacción de aldehídos o cetonas **[1]** con ácido cianhídrico **[2]** y son compuestos que contienen un grupo ciano y un hidroxilo sobre el mismo carbono.

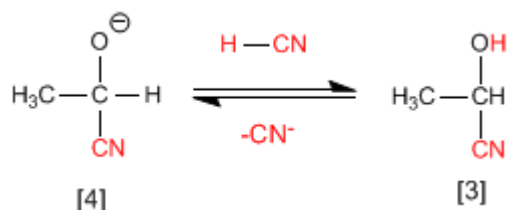


El mecanismo de la reacción transcurre en dos etapas:

**Etapas 1.** Los iones cianuro actúan como nucleófilos atacando al carbono carbonilo. El ácido cianhídrico es demasiado débil para generar cantidades importantes de cianuro, por ello, se añade cianuro de sodio o potasio al medio, garantizando la cantidad suficiente de cianuro para que la reacción transcurra en buen rendimiento.



**Etapas 2.** En este paso el ión alcóxido **[4]** se protona arrancando hidrógenos al ácido cianhídrico. En esta etapa se regeneran los iones cianuro.



### Kurt Alder (1902 - 1958)



**Origen:** Químico alemán.

**Lugar de nacimiento:** Königshütte (hoy Chorzów, Polonia).

**Formación:** estudió en la Universidad de Kiel. Bajo la supervisión del químico alemán Otto Diels, su jefe e instructor en Kiel.

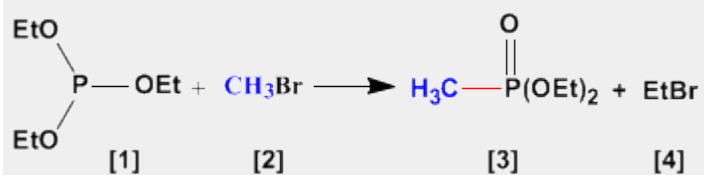
**Docencia:** Alder ejerció como profesor de química en las universidades de Kiel y Colonia.

**Investigación:** Alder se especializó en la síntesis diénica (conocida más tarde como la reacción Diels - Alder) que consiste fundamentalmente en el análisis y formación de compuestos orgánicos complejos. Ya en 1928 ambos fueron coautores de un ensayo sobre este proceso.

**Premio Nobel:** En 1950 recibió el Premio Nobel junto a Diels

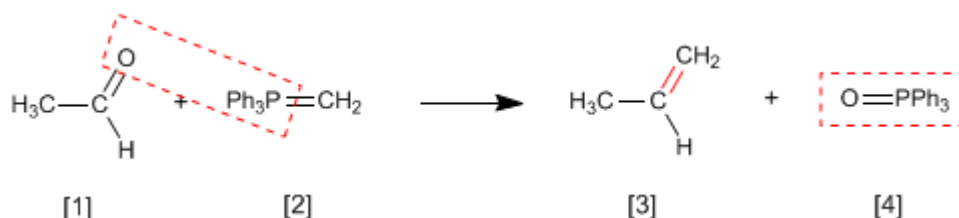
### Arbuzov (Reacción)

La reacción de Arbuzov se emplea en la síntesis de fosfonatos **[3]** a partir de fosfitos **[1]**. Los fosfonatos obtenidos en la síntesis de Arbuzov se emplean como materiales de partida en la síntesis de Horner-Wittig.



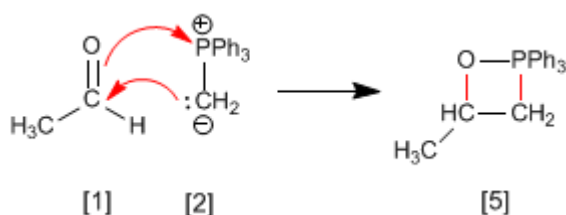
## Reacción de Wittig

La reacción de Wittig emplea iluros de fósforo [2] para transformar aldehídos y cetonas [1] en alquenos [3]. Como subproducto se obtiene el óxido de trifenilfosfina [4].

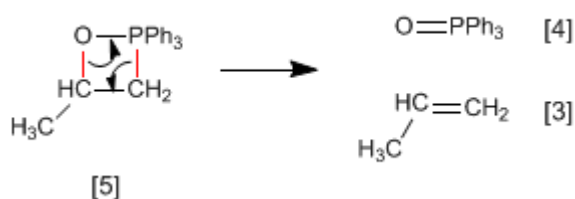


En el mecanismo de la reacción el iluro y el carbonilo se combinan para formar un oxafosfetano que rompe dejando libre el alqueno final.

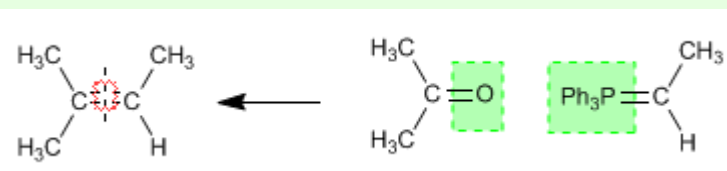
**Etapas 1.** El etanal y el iluro se combinan formando el fosfetano.



**Etapas 2.** El fosfetano rompe formando el alqueno y óxido de trifenilfosfina.



Ejemplo - Obtener mediante Wittig el 2-Metilbut-2-eno



Se rompe el alqueno por el doble enlace y a cada carbono se le agrega el grupo encerrado en verde.

Los **iluros de fósforo** se preparan mediante reacción de haloalcanos y trifenilfosfina, seguido de desprotonación del carbono con base fuerte (organometálicos de litio).



### Charles Friedel (1832 - 1899)



**Origen:** Químico frances..

**Lugar de nacimiento:** Estrasburgo.

**Formación:** estudió química en la Universidad de Berlín entre 1895 y 1899, consiguiendo el doctorado este año.

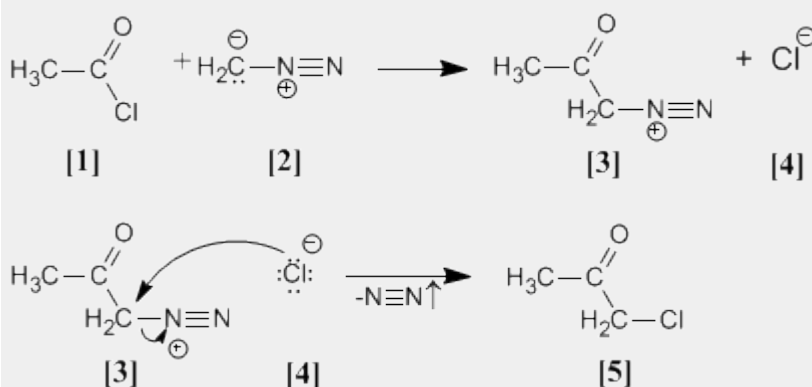
**Docencia:** Profesor en la Universidad de la Sorbona.

**Investigación:** Obtuvo el alcohol propílico. En 1877, Friedel y Crafts describieron por primera vez la reacción del benceno con un haloalcano en presencia de un ácido de Lewis. Esta reacción produce la alquilación del benceno y se conoce como alquilación de Friedl-Crafts.

**Premio Nobel:**

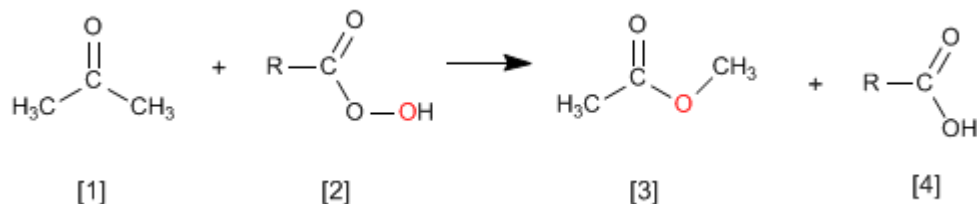
### Arndt Eistert (Síntesis)

Cloruro de acetilo **[1]** se trata con diazometano **[2]** rindiendo la sal de diazonio **[3]**. El cloruro **[4]** producido reacciona con la sal de diazonio para dar la  $\alpha$ -clorocetona **[5]**.

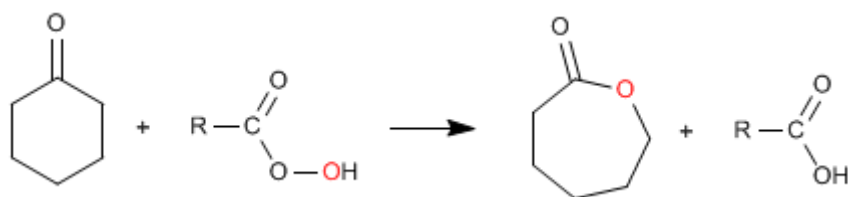


## Oxidación de Baeyer Villiger

La reacción de cetonas **[1]** con perácidos **[2]** produce ésteres **[3]**. El oxígeno del perácido se inserta entre el carbono carbonilo y el carbono alfa de la cetona. Esta reacción fue descrita por Adolf von Baeyer y Victor Villiger in 1899.

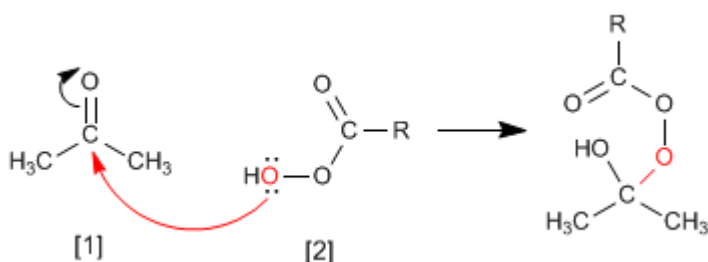


A partir de cetonas cíclicas se obtienen ésteres cíclicos (lactonas)

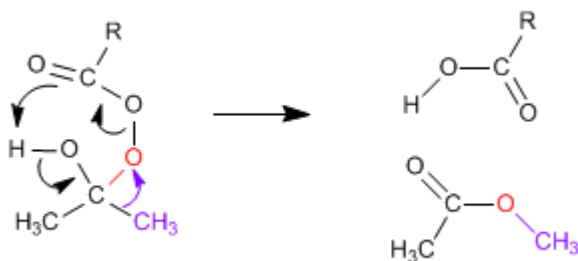


El mecanismo de Baeyer Villiger comienza con el ataque nucleófilo del perácido sobre el carbonilo, seguido de la migración del sustituyente desde el grupo carbonilo al oxígeno del perácido.

**Etapas 1.** Adición del perácido al carbonilo

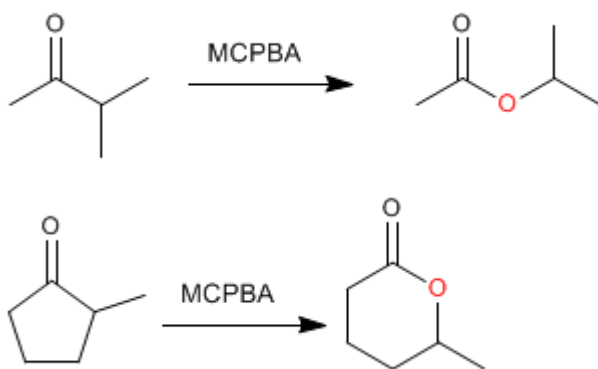


**Etapas 2.** Migración del sustituyente desde carbono carbonilo hacia el oxígeno (rojo)

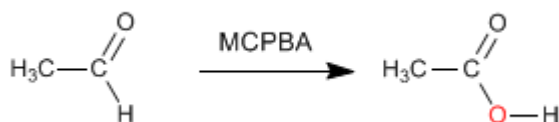


Cuando la cetona tiene dos sustituyentes diferentes migra mejor el más sustituido. Existe un orden de migración que nos ayuda a decidir que sustituyente pasa a unirse al oxígeno del perácido.

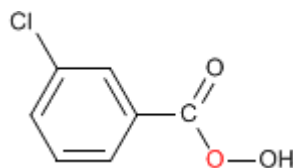
Orden de migración: H > carbono terciario > ciclohexilo > carbono secundario » fenilo > carbono primario > metilo



Como puede observarse en el orden de migración, el grupo que mejor migra, por su pequeño tamaño, es el hidrógeno, por ello, al tratar aldehídos con perácidos se produce la migración del hidrógeno formándose ácidos carboxílicos.



El **MCPBA** (Ácido meta-cloroperoxibenzoico) es un perácido ampliamente utilizado en la epoxidación de alquenos y también en Baeyer-Villiger. La fórmula del MCPBA se muestra a continuación.



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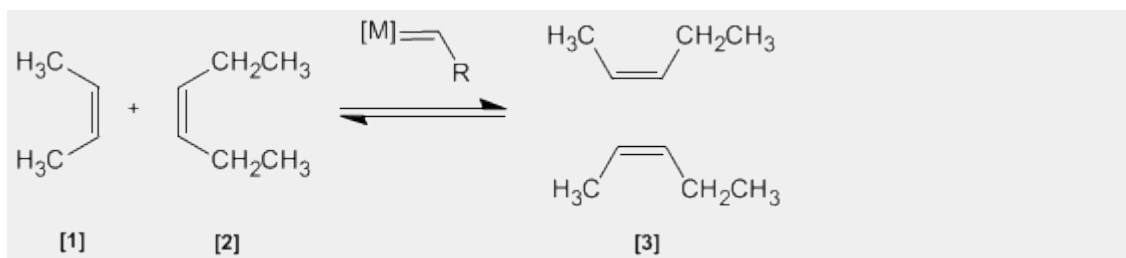
**Docencia:** Profesor en la Universidad de la Sorbona.

**Investigación:** Obtuvo el alcohol propílico. En 1877, Friedel y Crafts describieron por primera vez la reacción del benceno con un haloalcano en presencia de un ácido de Lewis. Esta reacción produce la alquilación del benceno y se conoce como alquilación de Friedl-Crafts.

**Premio Nobel:**

#### Metátesis de Alquenos

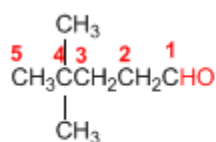
En esta reacción dos alquenos **[1]** y **[2]** son tratados con un metal de transición que actúa como catalizador, dando una mezcla de alquenos **[3]** (incluyendo isómeros Z/E). Este productos se obtiene por intercambio de grupos alquilideno.



## Nomenclatura de Aldehídos y Cetonas - Reglas IUPAC

**Regla 1.** Los aldehídos se nombran reemplazando la terminación **-ano** del alcano correspondiente por **-al**. No es necesario especificar la posición del grupo aldehído, puesto que ocupa el extremo de la cadena (localizador 1).

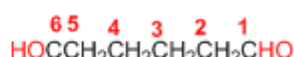
Cuando la cadena contiene dos funciones aldehído se emplea el sufijo **-dial**.



4,4-Dimetilpentanal

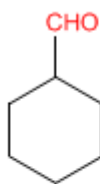


Hex-4-enal

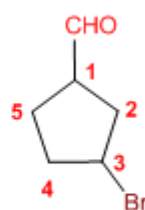


Hexanodial

**Regla 2.** El grupo **-CHO** se denomina **-carbaldehído**. Este tipo de nomenclatura es muy útil cuando el grupo aldehído va unido a un ciclo. La numeración del ciclo se realiza dando localizador 1 al carbono del ciclo que contiene el grupo aldehído.

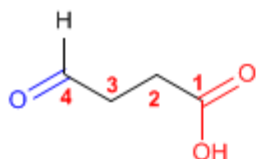


Ciclohexanocarbaldehído

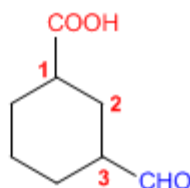


3-Bromociclopentanocarbaldehído

**Regla 3.** Cuando en la molécula existe un grupo prioritario al aldehído, este pasa a ser un sustituyente que se nombra como oxo- o formil-.



Ácido 4-oxobutanoico

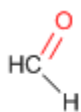


Ácido 3-formilciclohexanocarboxílico

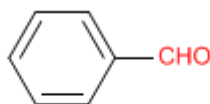
Tanto **-carbaldehído** como **formil-** son nomenclaturas que incluyen el carbono del grupo carbonilo. **-carbaldehído** se emplea cuando el aldehído es grupo funcional, mientras que **formil-** se usa cuando actúa de sustituyente.



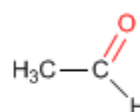
**Regla 4.** Algunos nombres comunes de aldehídos aceptados por la IUPAC son:



Formaldehído  
(Metanal)

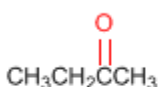


Benzaldehído  
(Benceno**carbaldehído**)

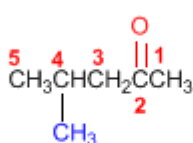


Acetaldehído  
(Etanal)

**Regla 5.** Las cetonas se nombran sustituyendo la terminación **-ano** del alcano con igual longitud de cadena por **-ona**. Se toma como cadena principal la de mayor longitud que contiene el grupo carbonilo y se numera para que éste tome el localizador más bajo.



Butan**ona**

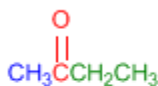


4-Metil-2-pentan**ona**

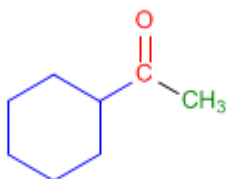


3-Metilciclohexan**ona**

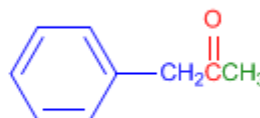
**Regla 6.** Existe un segundo tipo de nomenclatura para las cetonas, que consiste en nombrar las cadenas como sustituyentes, ordenándolas alfabéticamente y terminando el nombre con la palabra cetona.



Etil metil **cetona**

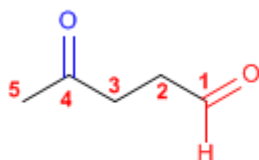


Ciclohexil metil **cetona**

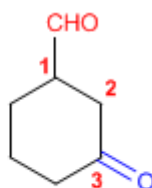


Fenil metil **cetona**

**Regla 7.** Cuando la cetona no es el grupo funcional de la molécula pasa a llamarse **OXO-**.



4-Oxopentan**al**

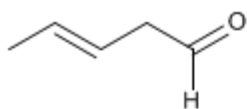


3-Oxociclohexano**carbaldehído**

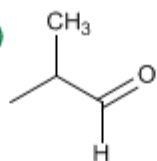
## Nomenclatura de Aldehídos y Cetonas - Problema 9.1

Nombra los siguientes aldehídos y cetonas:

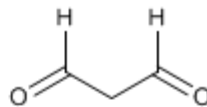
a)



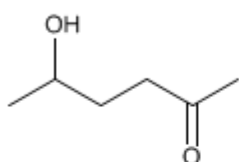
b)



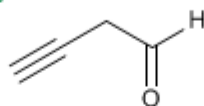
c)



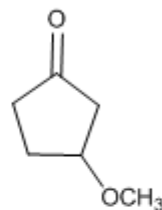
d)



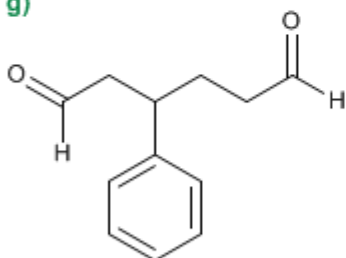
e)



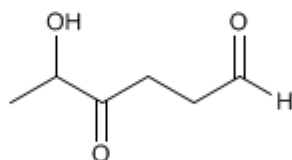
f)



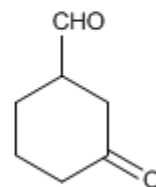
g)



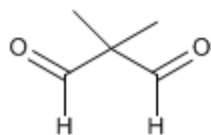
h)



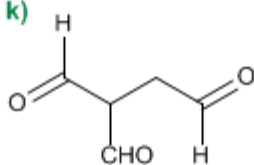
i)



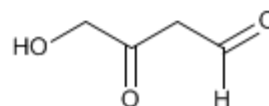
j)



k)

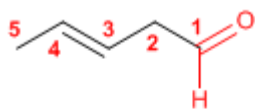


l)

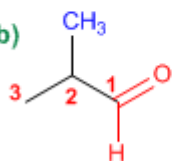


Solución

a)



b)



1. Cadena principal: 5 carbonos (pentano)

2. Numeración: comienza en el aldehído (grupo funcional)

Grupo funcional: aldehído

3. Nombre: Pent-3-enal

1. Cadena principal: 3 carbonos (propano)

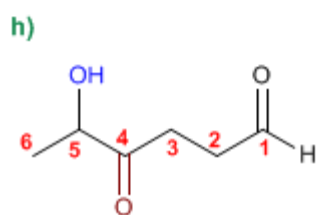
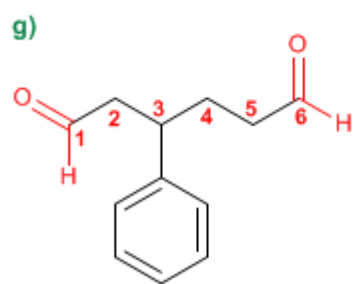
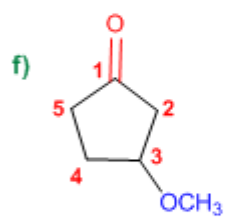
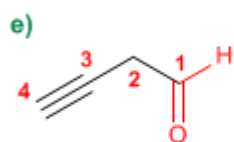
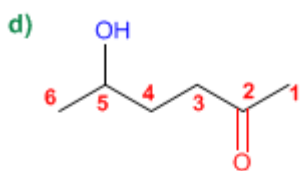
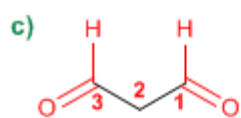
2. Numeración: localizador más bajo al aldehído.

3. Grupo funcional: aldehído

4. Sustituyentes: metilo en 2.

5. Nombre: 2-Metilpropanal

Los aldehídos y cetonas son prioritarios sobre alquenos y alquinos, y se numeran otorgándoles el localizador más bajo



1. Cadena principal: 3 carbonos (propano)
2. Grupo funcional: aldehído (dialdehído)
3. Nombre: Propanodial

1. Cadena principal: 6 carbonos (hexano)
2. Grupo funcional: cetona
3. Numeración: asignar el menor localizador a la cetona
4. Sustituyentes: hidroxí en 5.
5. Nombre: 5-Hidroxihexan-2-ona

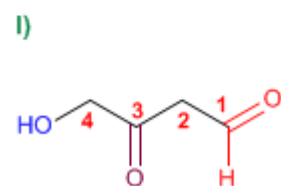
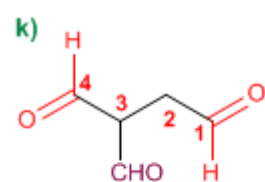
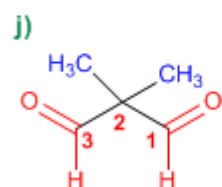
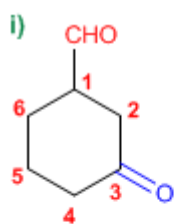
1. Cadena principal: 4 carbonos (butano)
2. Grupo funcional: aldehído
3. Numeración: asignar el menor localizador al aldehído
4. Nombre: But-3-inal

1. Cadena principal: ciclo de 5 miembros (ciclopentano)
2. Grupo funcional: cetona
3. Numeración: comienza en la cetona y prosigue hacia el sustituyente
4. Sustituyentes: metoxi en 3.
5. Nombre: 3-Metoxiciclopentanona

1. Cadena principal: 6 carbonos (hexano)
2. Grupo funcional: aldehído (dialdehído)
3. Numeración: comienza en el extremo que otorga al fenilo el localizador más bajo.
4. Sustituyentes: fenilo en 3.
5. Nombre: 3-Fenilhexanodial

1. Cadena principal: 6 carbonos (hexano)
2. Grupo funcional: aldehído
3. Numeración: asignar el menor localizador al aldehído
4. Sustituyentes: hidroxí en 5 y oxo en 4.
5. Nombre: 5-Hidroxí-4-oxohexanal

Los aldehídos son prioritarios sobre las cetonas que pasan a nombrarse como sustituyentes (oxo-)



1. Cadena principal: ciclo de 6 miembros (ciclohexano)
2. Grupo funcional: aldehído (-carbaldehído)
3. Numeración: menor localizador al grupo -CHO (este no se numera)
4. Sustituyentes: cetona (oxo-) en 3
5. Nombre: 3-Oxociclohexanocarbaldehído

1. Cadena principal: 3 carbonos (propano)
2. Grupo funcional: aldehído (dialdehído)
3. Sustituyentes: metilos en 2,2.
4. Nombre: 2,2-Dimetilpropanodial

1. Cadena principal: 4 carbonos (butano)
2. Grupo funcional: aldehído
3. Sustituyentes: formil en 3
4. Nombre: 3-Formilbutanodial

1. Cadena principal: 4 carbonos (butano)
2. Grupo funcional: aldehído
3. Numeración: asignar el menor localizador al aldehído
4. Sustituyentes: hidroxil en 4 y oxo en 3.
5. Nombre: 4-Hidroxil-3-oxobutanal

## Nomenclatura de Aldehídos y Cetonas - Problema 9.2

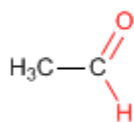
PRINT EMAIL

Dibuja la estructura de los siguientes aldehídos y cetonas:

- |   |                                  |
|---|----------------------------------|
| a) Etanal (acetaldehído)                          | g) 2,5-Dioxooctanodial           |
| b) 3-Metilbutanal                                 | h) 1,3-Ciclohexanodiona          |
| c) Benzaldehído                                   | i) 3-Metil-3-pental              |
| d) 4-Hidrox ciclohexanocarbaldehído               | j) 3-Oxobutanal                  |
| e) 3-Hidroxi-4-metil-5-oxociclohexanocarbaldehído | k) 3-Hidrox ciclopentanona       |
| f) 2-Metil-2,5-octanodiona                        | l) 4-Etoxi-5-fenil-3-oxoheptanal |

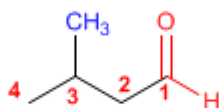
Solución

a)



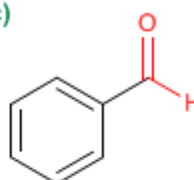
Etanal (acetaldehído)

b)

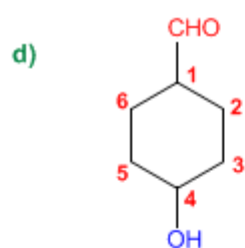


3-Metilbutanal

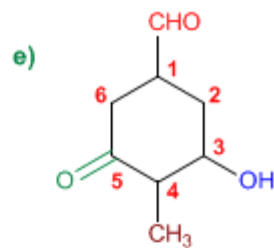
c)



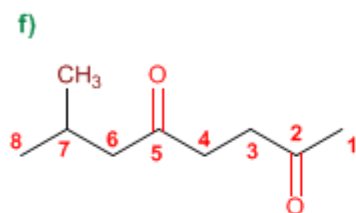
Benzaldehído



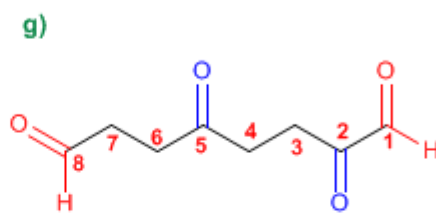
4-Hidroxiciclohexanocarbaldehído



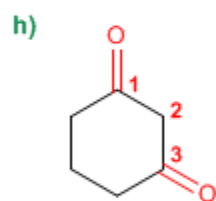
3-Hidroxi-4-metil-5-oxociclohexanocarbaldehído



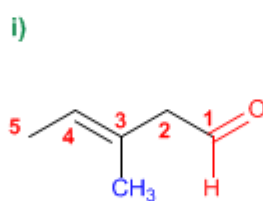
7-Metil-2,5-octanodiona



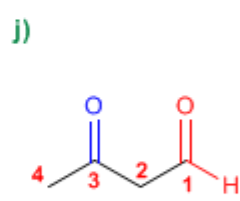
2,5-Dioxooctanodial



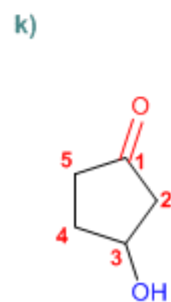
1,3-Ciclohexanodiona



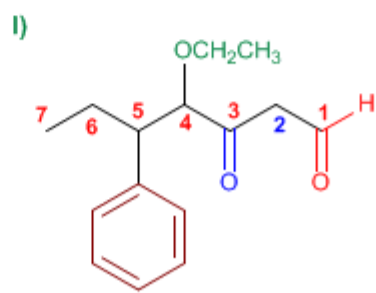
3-Metil-3-pentenal



3-Oxobutanal



3-Hidroxiciclopentanona



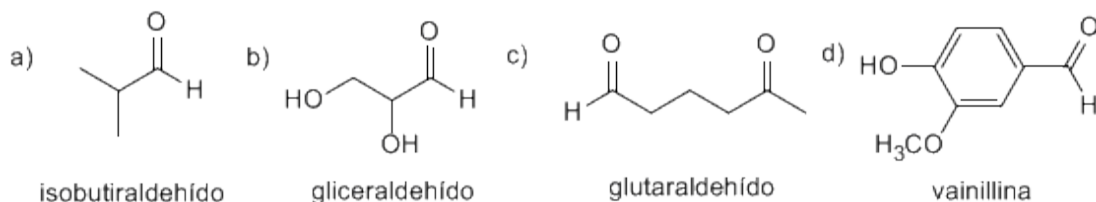
4-Etoxi-5-fenil-3-oxoheptanal



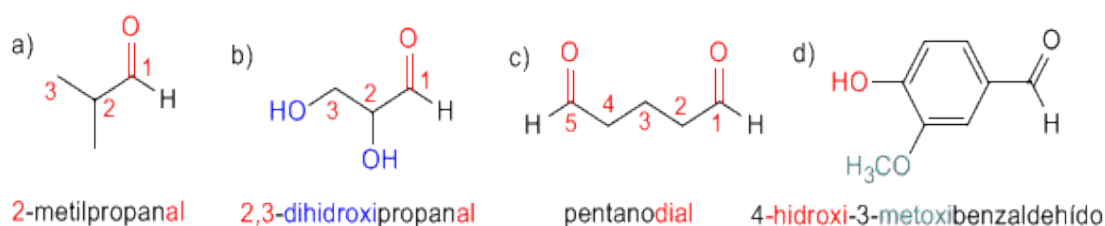
# PROBLEMAS RESUELTOS DE ALDEHÍDOS Y CETONAS

## Aldehídos y Cetonas: Problema 1

1) A continuación se dan nombres comunes y las fórmulas estructurales de algunos compuestos carbonílicos. Indique el nombre correspondiente según la IUPAC.



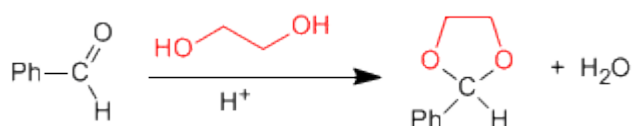
Solución



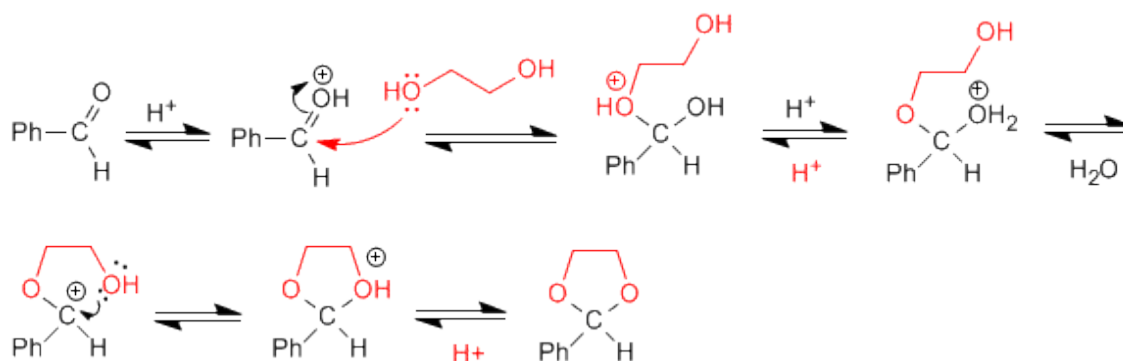
## Aldehídos y cetonas: Problema 2

Dibuje la estructura del acetal que se forma cuando el benzaldehído se calienta con 1,2-etanodiol en medio ácido. Escriba un mecanismo detallado que justifique su formación. Describa paso a paso la hidrólisis de este acetal en medio ácido acuoso.

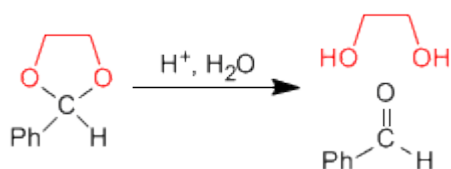
SOLUCIÓN



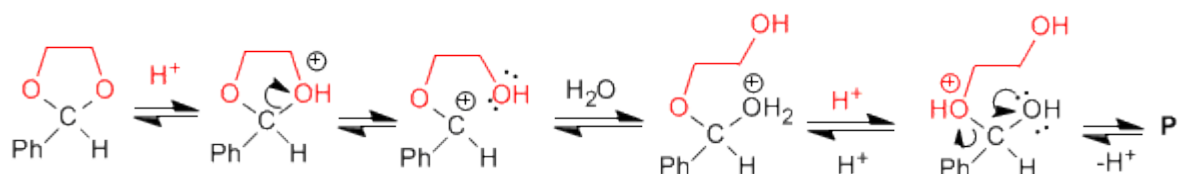
Mecanismo de formación del acetal:



La hidrólisis del acetal en medio ácido acuoso sigue es etapas inversas a la síntesis.



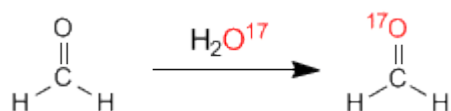
Mecanismo de hidrólisis del acetal cíclico.



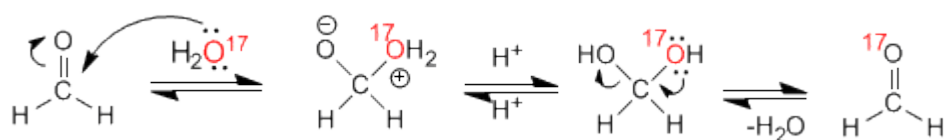
### Aldehídos y Cetonas: Problema 3

Cuando se disuelve formaldehído en agua marcada con  $^{17}\text{O}$ , se observa que después de unas horas tanto el hidrato del formaldehído como el formaldehído han incorporado el isótopo  $^{17}\text{O}$ . Sugiera una explicación razonable de este hecho.

SOLUCION



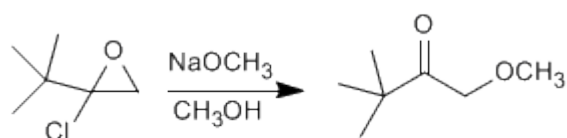
Mecanismo:



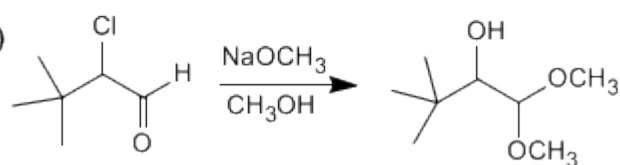
### Aldehídos y Cetonas: Problema 4

Sugiera un mecanismo razonable para una de las siguientes reacciones:

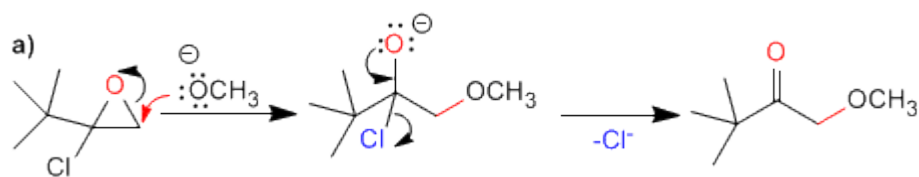
a)



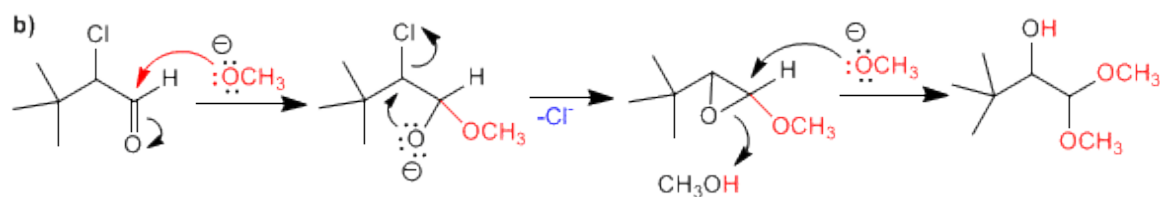
b)



## SOLUCION



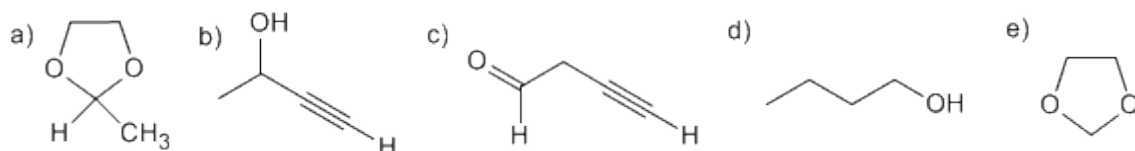
La primera etapa consiste en la apertura del oxaciclopropano sobre el carbono menos sustituido. En la segunda etapa, la cesión del par del oxígeno elimina el cloro, formándose un carbonilo.



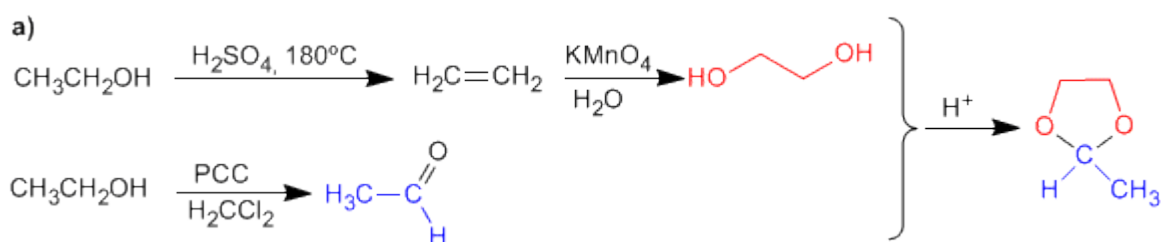
En el primer paso hay dos posibles posiciones de ataque; el carbono carbonilo y el carbono del cloro. Como el producto final no tiene metóxido en el carbono del cloro, atacamos al carbonilo. En la segunda etapa se produce una sustitución nucleófila intramolecular. Para terminar el metóxido abre el epóxido.

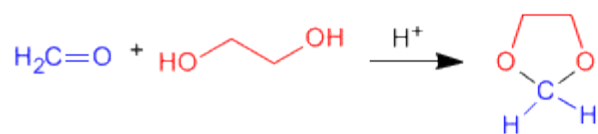
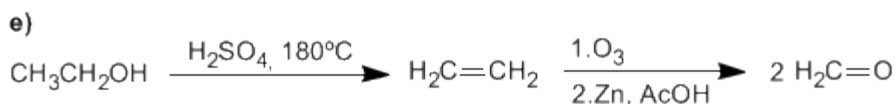
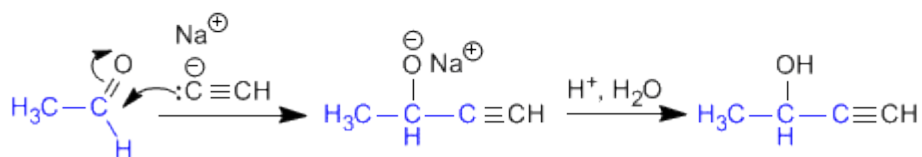
## Aldehídos y Cetonas: Problema 5

Usando etanol como fuente de todos los átomos de carbono y los reactivos que necesite, describa una síntesis eficiente de cada una de las sustancias siguientes:

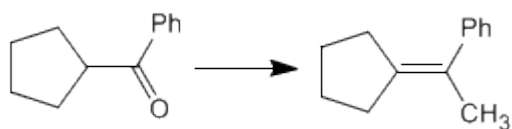


## SOLUCIÓN





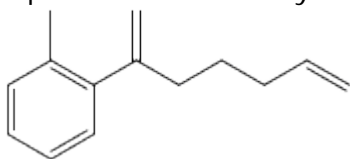
Utilizando los reactivos necesarios, indicar las etapas que permiten realizar la siguiente transformación:



[2] Isomerización en medio ácido, impulsada por la mayor estabilidad del alqueno interno.

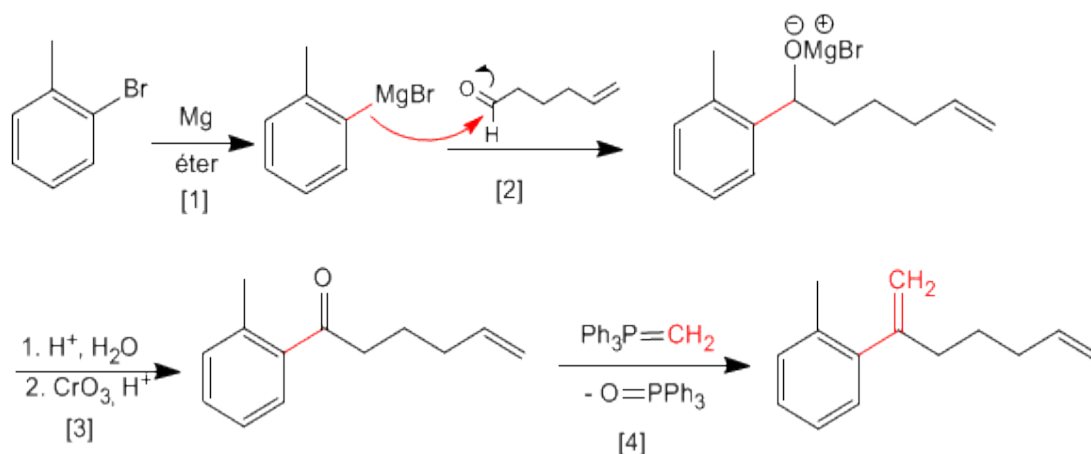
## Aldehídos y Cetonas: Problema 7

A partir de 5-hexenal y o-bromotolueno obtener el siguiente producto.



Pueden ser necesarios reactivos orgánicos e inorgánicos adicionales.

SOLUCIÓN



[1] Formación del magnesiano

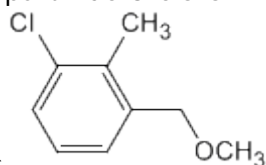
[2] Ataque nucleófilo del magnesiano al carbonilo.

[3] Hidrólisis y posterior oxidación del alcohol secundario.

[4] Reacción de Wittig entre la cetona y el trifenilmetilenfosforano.

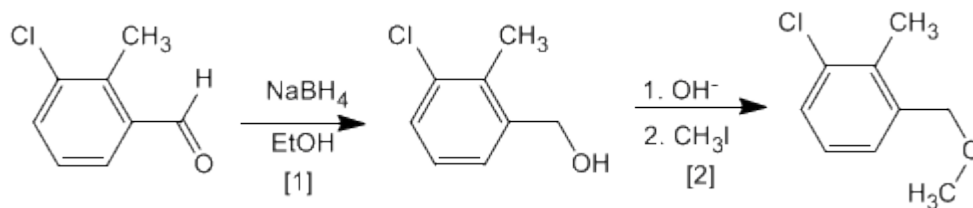
## Aldehídos y Cetonas: Problema 8

Obtener a partir de 3-cloro-2-metilbenzaldehído y de los reactivos



necesarios  
el compuesto siguiente:

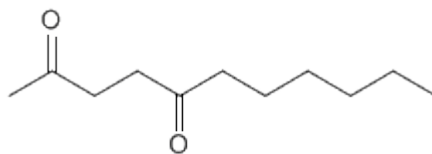
SOLUCIÓN



[1] Reducción del aldehído a alcohol

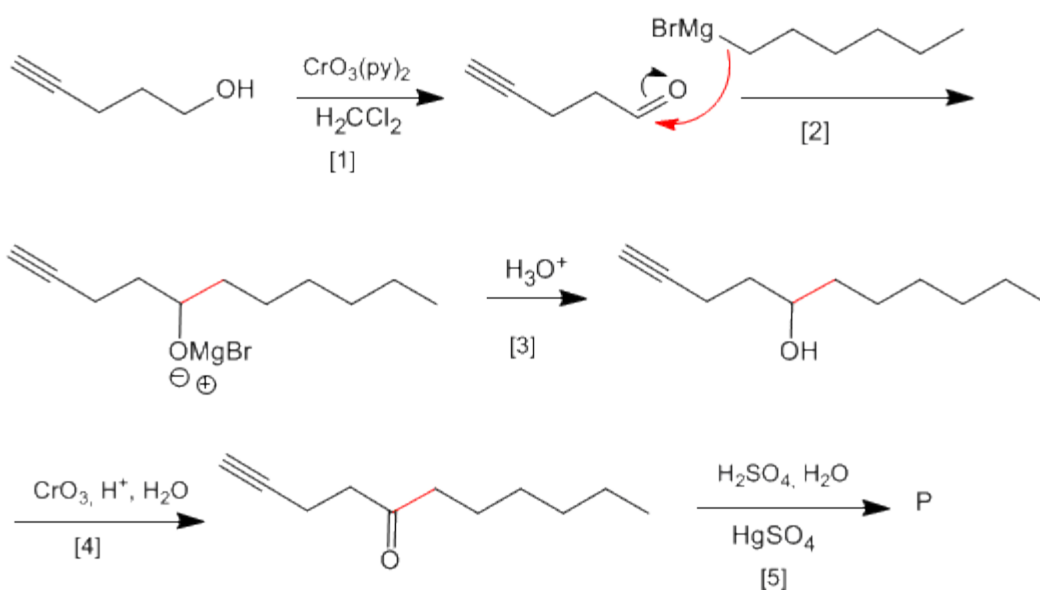
[2] Síntesis de Williamson de éteres.

## Aldehídos y Cetonas: Problema 9



A partir de 4-pentin-1-ol obtener:

SOLUCIÓN

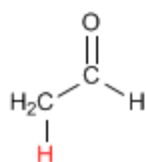


- [1] Oxidación del alcohol a aldehído
- [2] Formación del enlace carbono-carbono mediante organometálicos de magnesio
- [3] Protonación del alcohol
- [4] Oxidación del alcohol con Jones (Puedes utilizar también  $\text{CrO}_3(\text{py})_2$ )
- [5] Hidratación Markovnikov del alquino, para formar cetonas

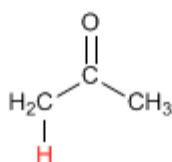
# TEORÍA DE ENOLES Y ENOLATOS

## Formación de Enolatos

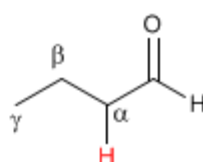
Los aldehídos y cetonas presentan hidrógenos ácidos en la posición vecina al grupo carbonilo, conocida como posición alfa. Estos hidrógenos presentan un pKa comprendido entre 18 y 21.



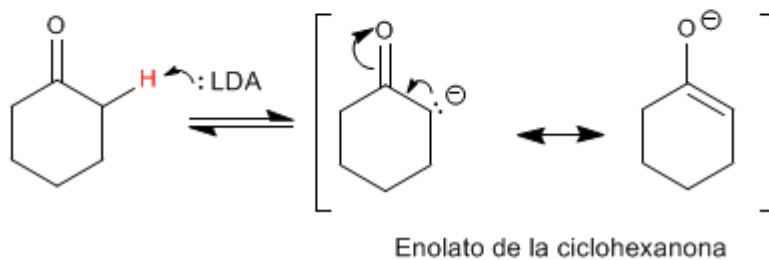
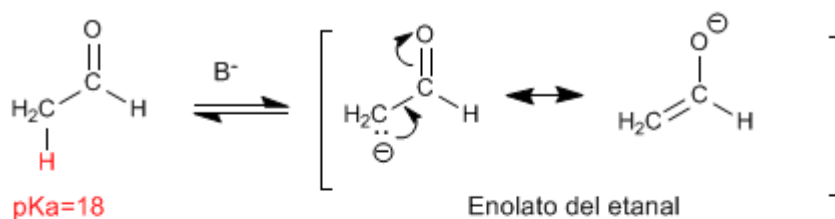
pKa=18



pKa=20-21



La acidez de los hidrógenos  $\alpha$  es debida a la estabilización de la base conjugada (enolato) por resonancia.

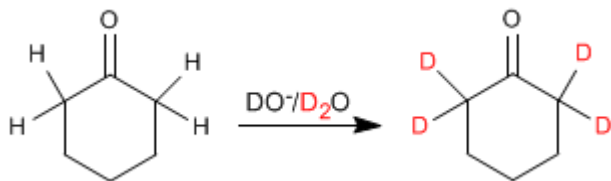






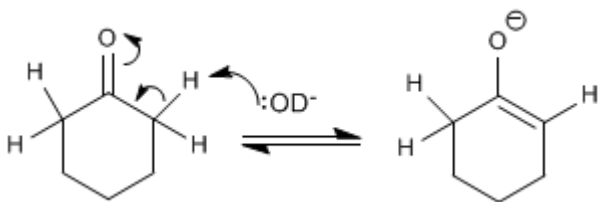
## Intercambio hidrógeno - Deuterio

Los aldehídos y cetonas intercambian sus hidrógenos a por deuterios cuando se tratan con  $\text{DO}^-/\text{D}_2\text{O}$  o con  $\text{D}^+/\text{D}_2\text{O}$ . En medios básicos la reacción transcurre a través de enolatos y en medios ácidos los intermediarios formados son enoles.

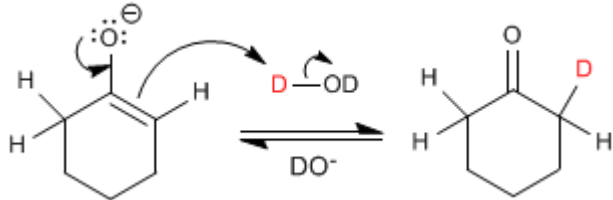


El mecanismo del intercambio hidrógeno-deuterio transcurre en los siguientes pasos:

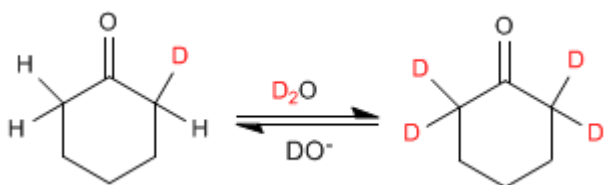
**Etapas 1.** Formación del enolato



**Etapas 2.** Transferencia del deuterio al enolato



**Etapas 3.** Sustitución del resto de hidrógenos



## Halogenación de aldehídos y cetonas

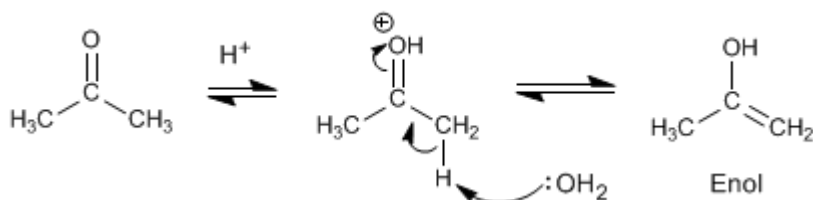
Los aldehídos y cetonas reaccionan con halógenos en medios ácidos o básicos produciéndose la sustitución de hidrógenos a por halógenos.

Halogenación de la propanona en medio ácido:

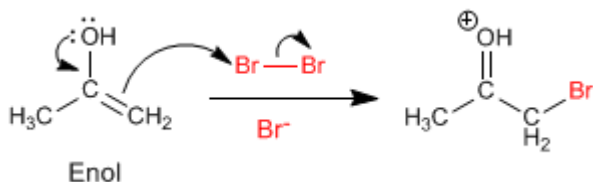


El mecanismo de halogenación en **medio ácido** tiene las siguientes etapas:

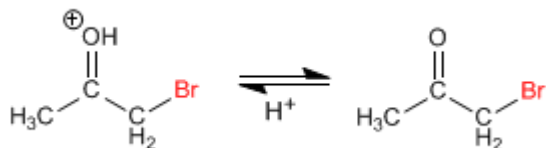
**Etapas 1.** Formación del enol



**Etapas 2.** Ataque nucleófilo del enol sobre el halógeno ayudado por la cesión del par del oxígeno.

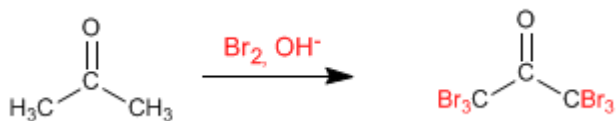


**Etapas 3.** Desprotonación



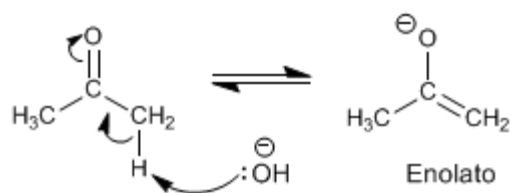
Trabajando con un equivalente de reactivo la halogenación para en una primera adición y no ocurren polihalogenaciones. El paso clave del mecanismo es la formación del enol y esta etapa requiere protonar el oxígeno del carbonilo. Una vez halogenada la posición  $\alpha$  el oxígeno se vuelve menos básico, debido al efecto electronegativo del bromo, protonándose peor.

Halogenación de la propanona en **medio básico**:

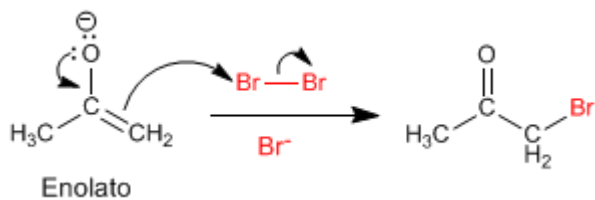


La halogenación en medio básico tiene el siguiente mecanismo:

**Etapla 1.** Formación del enolato



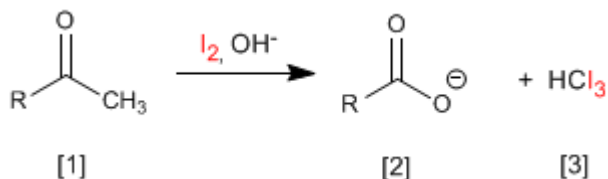
**Etapla 2.** Ataque nucleófilo del enolato sobre el halógeno ayudado por la cesión del para del oxígeno.



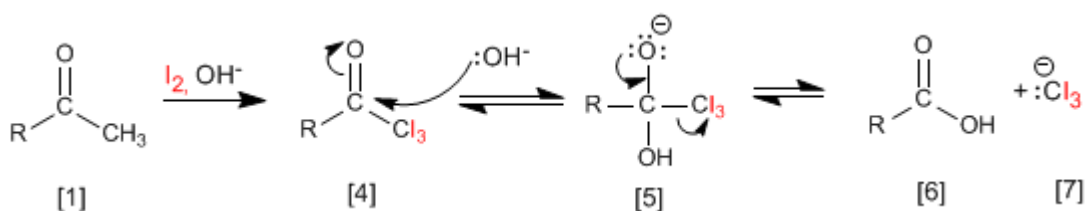
Este mecanismo se repite otras 5 veces sustituyendo todos los hidrógenos a por halógenos. En este caso la reacción no para puesto que el producto halogenado es más reactivo que la propanona de partida. La base arranca mejor los hidrógenos en el producto halogenado (son más ácidos), haciendo imposible parar la reacción.

## Reacción del Haloformo (Yodoformo)

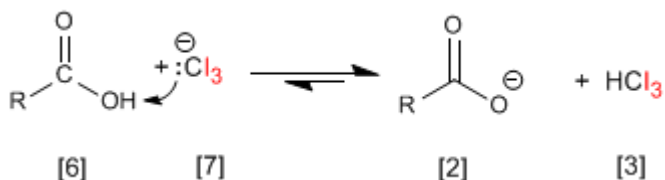
Las cetonas metílicas **[1]** reaccionan con halógenos en medios básicos generando carboxilatos **[2]** y haloformo **[3]**.



El mecanismo consiste en halogenar completamente el metilo, sustituyendo en una etapa posterior el grupo  $-\text{CX}_3$  formado por  $-\text{OH}$ .



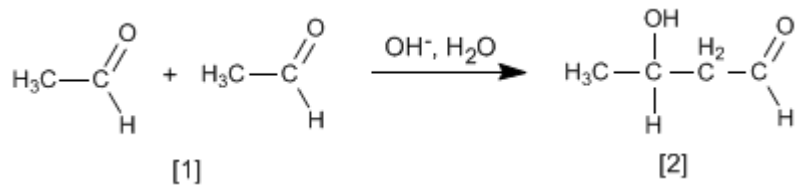
El grupo  $\text{Cl}_3^\ominus$  es muy básico y desprotona el ácido carboxílico formándose yodoformo y el carboxilato.



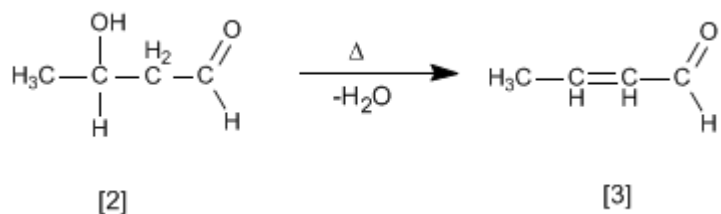
Esta reacción (con yodo) puede emplearse como ensayo analítico para identificar cetonas metílicas aprovechando que el yodoformo precipita de color amarillo.

## Condensación Aldólica

Aldehídos y cetonas [1] condensan en medios básicos formando aldoles [2]. Esta reacción se denomina condensación aldólica.

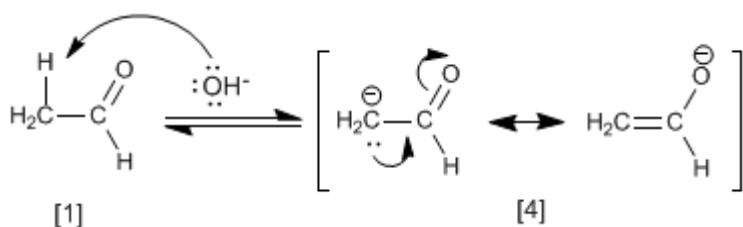


El aldol [2] formado deshidrata en el medio básico por calentamiento para formar un  $\alpha,\beta$ -insaturado [3].



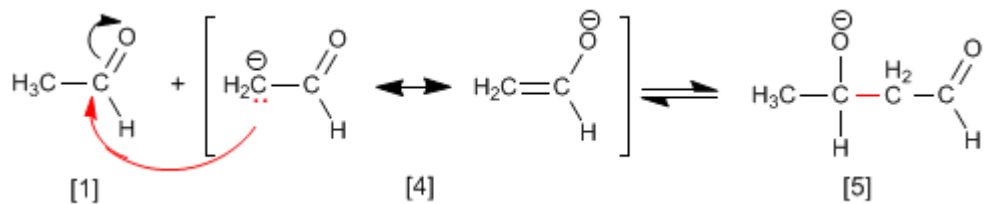
El mecanismo de la condensación aldólica transcurre con formación de un enolato, que ataca al carbonilo de otra molécula. En esta condensación se forma un enlace carbono-carbono entre el carbonilo de una molécula y el carbono  $\alpha$  de la otra.

### Etapa 1. Formación del enolato

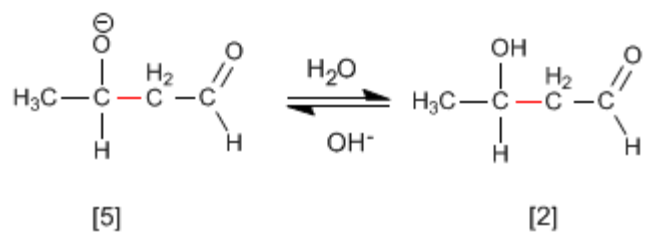


La base desprotona el carbono alfa del etanal [1] generando el enolato [4] estabilizado por resonancia.

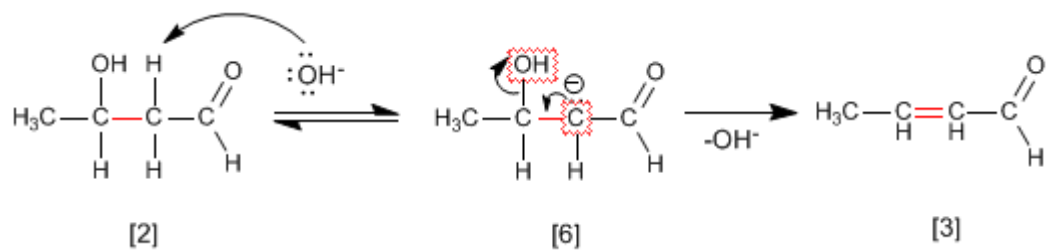
### Etapa 2. Ataque nucleófilo del enolato sobre el carbonilo



**Etapas 3.** Protonación

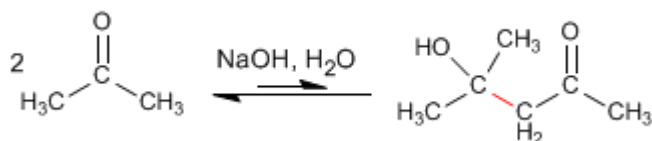


**Etapas 4.** Deshidratación del aldol

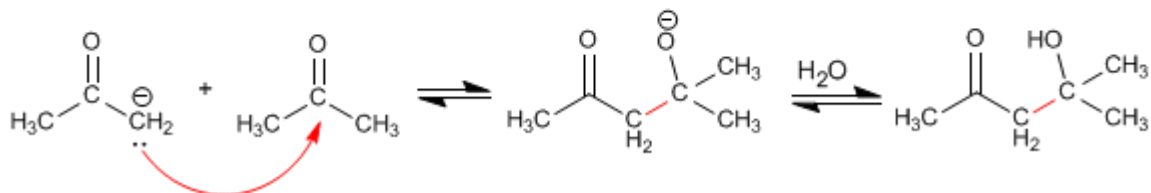
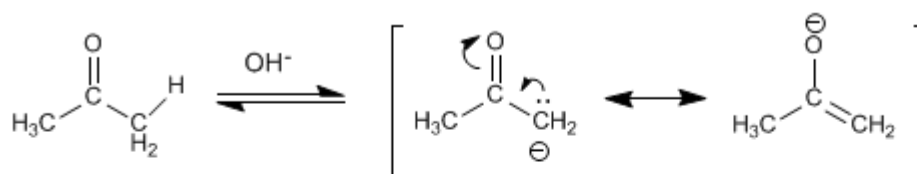


## Condensación aldólica con cetonas

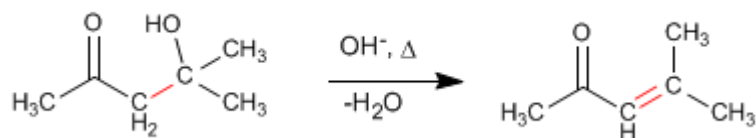
Las cetonas son menos reactivas que los aldehídos y dan un rendimiento muy bajo en la condensación aldólica. Así, dos moléculas de propanona condensan para formar el aldol correspondiente con un rendimiento del 2%. Se pueden conseguir porcentajes elevados del producto separándolo del medio de reacción según se va formando, o bien, calentando para deshidratarlo. De ambas formas los equilibrios de la aldólica se desplazan hacia el producto final.



**Mecanismo de la reacción:**



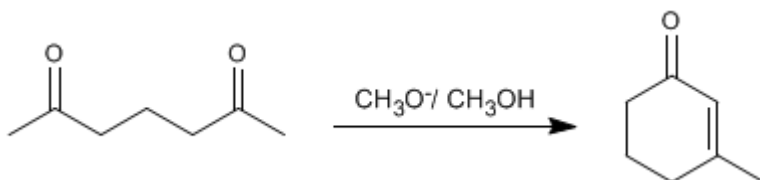
La deshidratación final permite el desplazamiento de los equilibrios. También se puede realizar una extracción del aldol del medio de reacción para favorecer la reacción.



## Condensación aldólica intramolecular

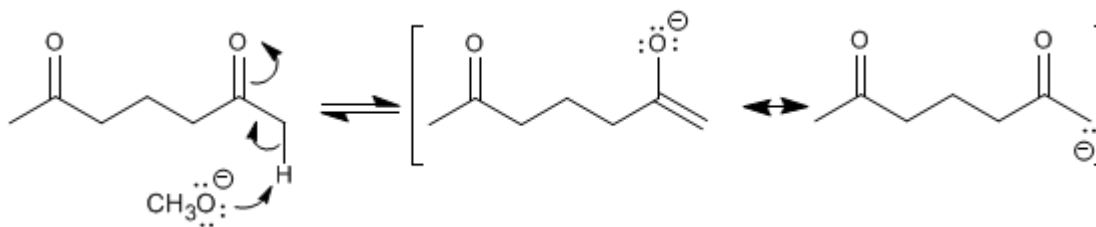
Los compuestos dicarbonílicos condensan mediante la aldólica intramolecular en medios básicos. En esta reacción se obtienen ciclos de cinco o seis miembros.

Así, la 2,6-heptanodiona condensa con metóxido en metanol para formar el 3-metilciclohex-2-enona.

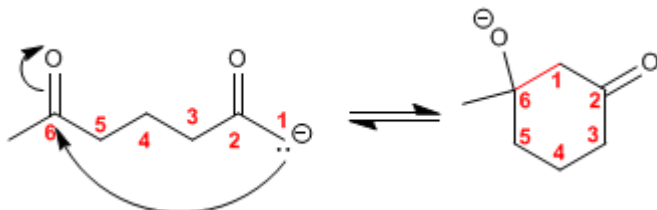


El mecanismo de la reacción transcurre a través de las siguientes etapas:

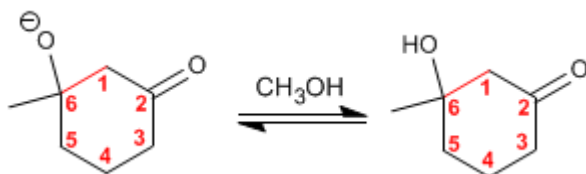
**Etapas 1.** Formación del enolato.



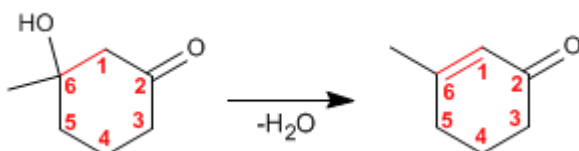
**Etapas 2.** Adición nucleófila intramolecular



**Etapas 3.** Protonación de la base del aldol



**Etapas 4.** Deshidratación del aldol



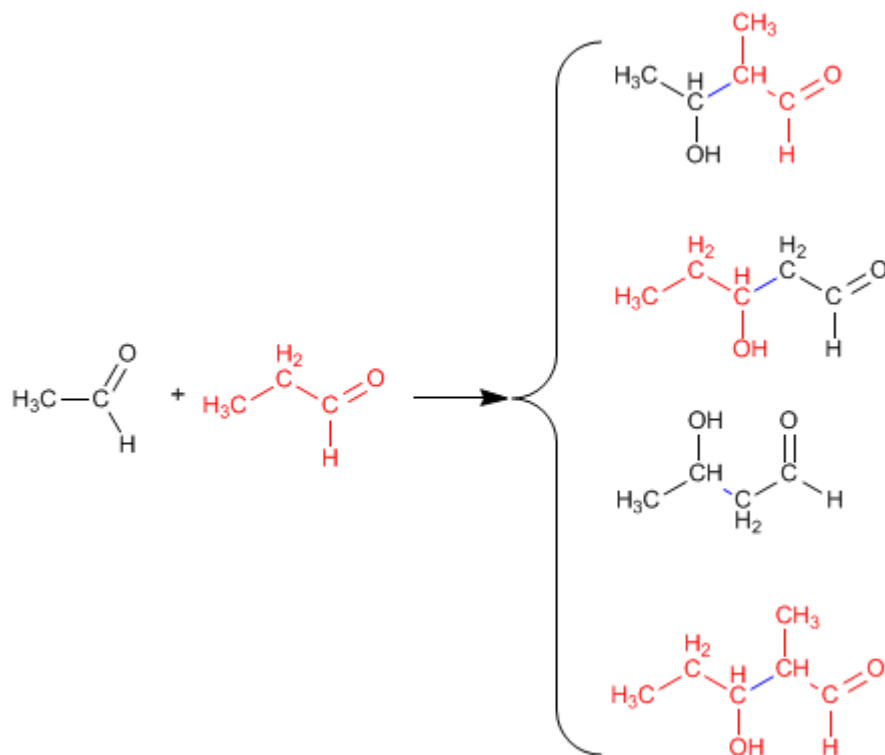


## Condensación aldólica cruzada o mixta

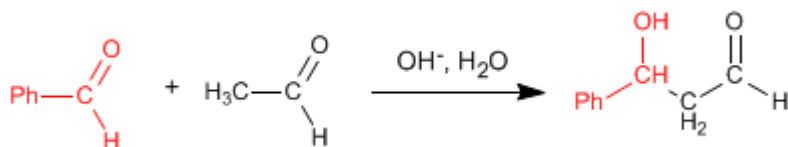
La reacción entre dos carbonilos diferentes se llama aldólica cruzada o mixta. Esta reacción sólo tiene utilidad sintética en dos casos:

1. Sólo uno de los carbonilos puede formar enolatos.
2. Uno de los carbonilos es mucho más reactivo que el otro.

En el resto de situaciones la aldólica mixta genera mezclas de cuatro productos. Veamos como ejemplo la condensación del etanal y propanal.

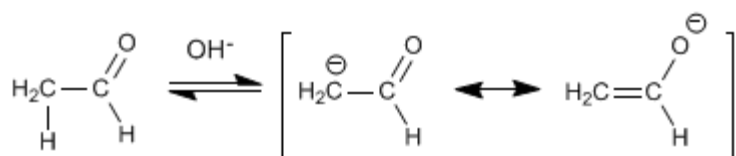


La condensación aldólica mixta del etanal con el benzaldehído genera un producto, cuando se trabaja en exceso de benzaldehído, debido a que el benzaldehído carece de hidrógenos en el carbono alfa y no puede formar enolatos.



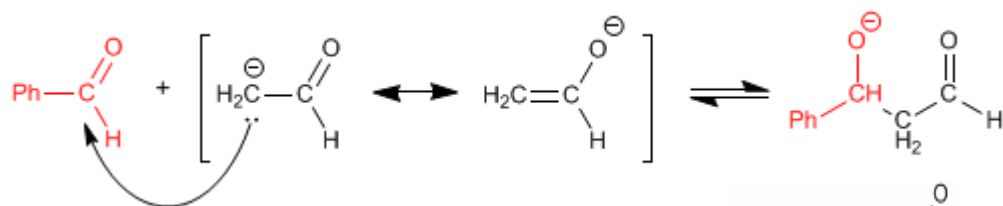
El mecanismo de esta reacción tiene lugar en las siguientes etapas:

### Etapla 1. Enolización del etanal

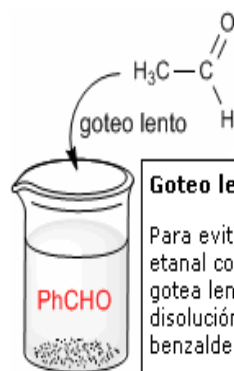


La formación de enolatos sólo puede tener lugar con el etanal, puesto que el benzaldehído carece de hidrógenos ácidos en el carbono alfa.

### Etapla 2. Ataque nucleófilo del enolato al benzaldehído.



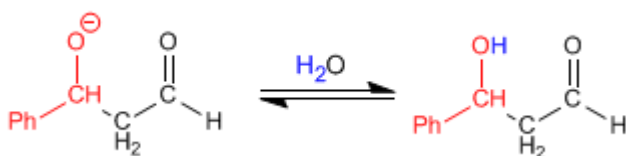
En esta etapa puede ocurrir el ataque del enolato de etanal sobre si mismo. Para evitarlo debe trabajarse en exceso de benzaldehído. Un procedimiento experimental muy usado para evitar la condensación del etanal consigo mismo es gotear lentamente el etanal sobre una disolución básica de benzaldehído



#### Goteo lento

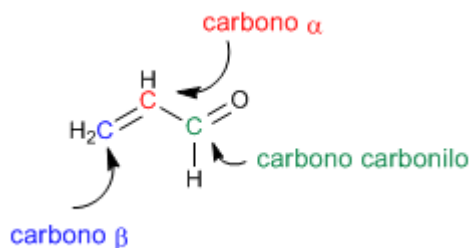
Para evitar la condensación del etanal consigo mismo, se gotea lentamente sobre una disolución básica de benzaldehído.

### Etapla 3. Protonación



## Síntesis de carbonilos alfa,beta-insaturados

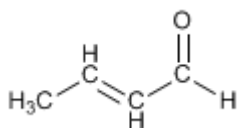
Los carbonilos  $\alpha,\beta$ -insaturados son compuestos orgánicos que tienen un doble enlace entre las posiciones  $\alpha,\beta$  de un aldehído o cetona.



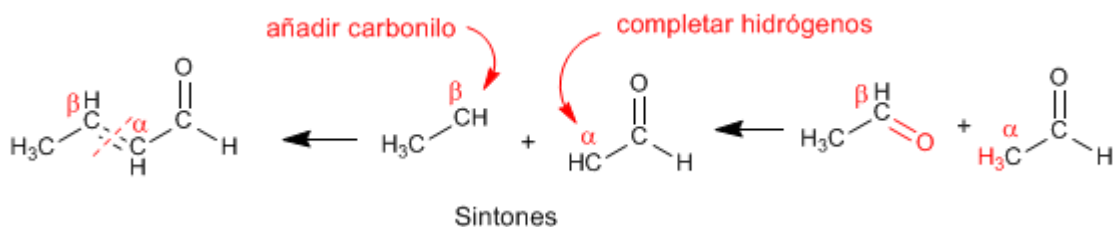
El propenal o acroleína es un carbonilo  $\alpha,\beta$ -insaturado. Sus dos dobles enlaces conjugados le confieren una reactividad especial.

Existen 4 métodos importantes para la preparación de  $\alpha,\beta$ -insaturados: condensación aldólica, halogenación del carbono  $\alpha$  seguida de eliminación, oxidación de alcoholes alílicos y Wittig.

**Método 1.** Preparar mediante la condensación aldólica el siguiente compuesto.

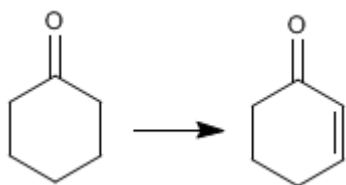


Empleamos la retrosíntesis para preparar el compuesto. Al ser de la familia de los  $\alpha,\beta$ -insaturados se puede obtener mediante la condensación aldólica.

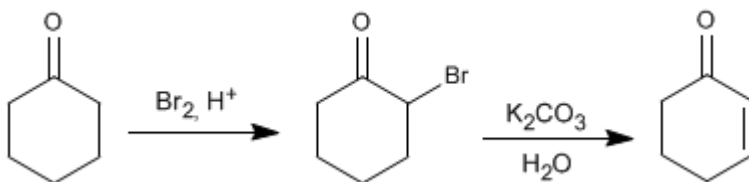


Para obtener los reactivos que forman el  $\alpha,\beta$ -insaturado se rompe por el doble enlace, obteniéndose los sintones (equivalentes sintéticos). Los reactivos se obtienen añadiendo al carbono  $\beta$  un carbonilo y completando los hidrógenos que faltan en el carbono  $\alpha$ .

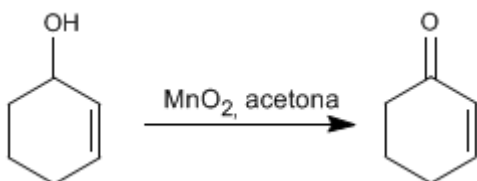
**Ejemplo 2.** Indicar como se puede realizar la siguiente transformación.



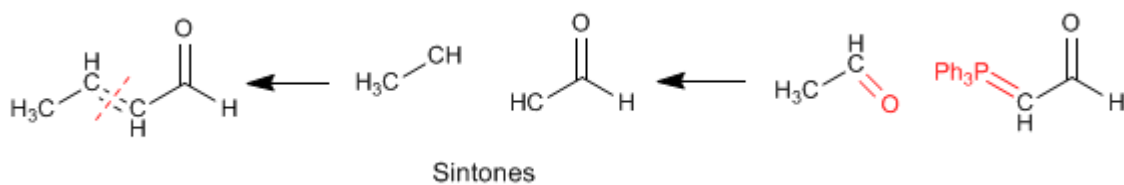
En una primera etapa se halogena la posición  $\alpha$  del carbonilo. En la segunda etapa se realiza una eliminación que nos deja el producto final.



**Método 3.** La oxidación de alcoholes alílicos con dióxido de manganeso en acetona produce  $\alpha,\beta$ -insaturados



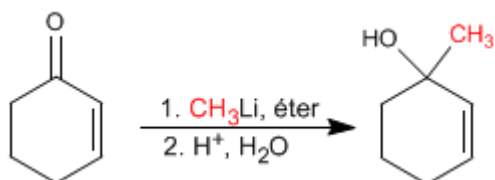
**Método 4.** Reacción de Wittig



## Reactividad de carbonilos alfa,beta-insaturados

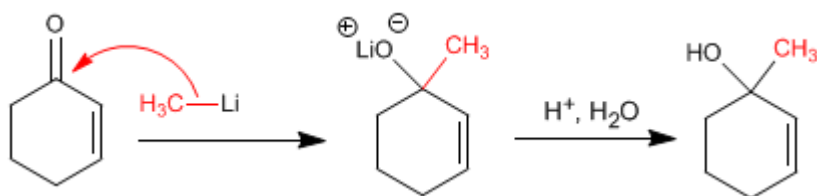
Los  $\alpha,\beta$ -insaturados son compuestos que poseen dos posiciones electrófilas: el carbono carbonilo y el carbono  $\beta$ .

**Adiciones 1,2.** Los organometálicos de litio atacan al carbono carbonilo dando lugar a adiciones 1,2.



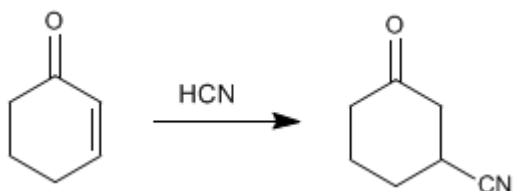
Los organometálicos de litio y magnesio atacan al carbono carbonilo de los  $\alpha,\beta$ -insaturados

Mecanismo de la adición 1,2

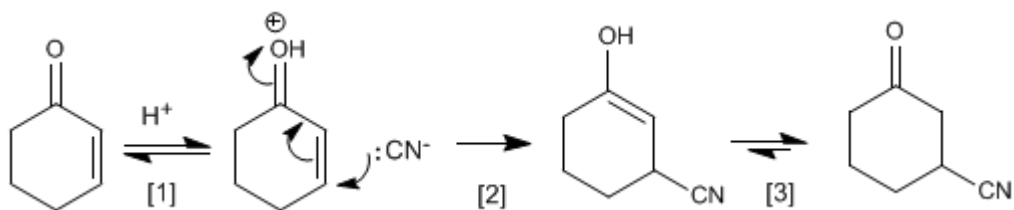


**Adiciones 1,4.** Los cupratos, cianuro y otros nucleófilos atacan al carbono  $\beta$  de los  $\alpha,\beta$ -insaturados, dando adiciones 1,4.

El ácido cianhídrico da adiciones 1,4 con los  $\alpha,\beta$ -insaturados. El ciano se une al carbono  $\beta$ .

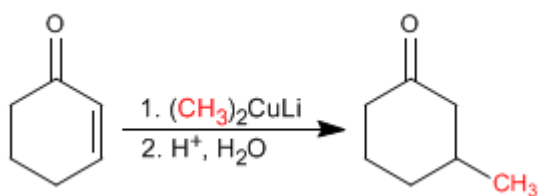


Mecanismo de adición del ácido cianhídrico a la Ciclohex-2-enona

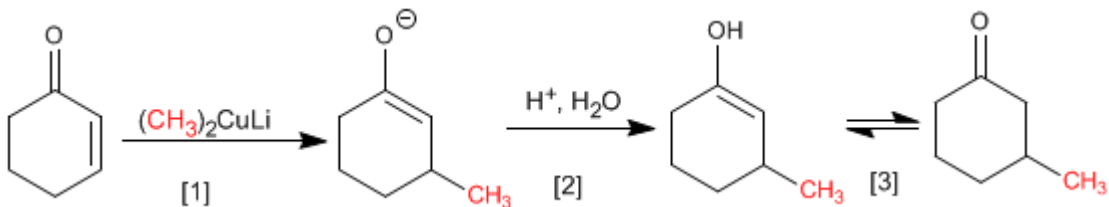


- [1] Protonación del carbonilo
- [2] Ataque nucleófilo del cianuro al carbono  $\beta$ .
- [3] Tautomería ceto-enol.

Los cupratos son organometálicos de cobre que se adicionan al carbono  $\beta$  de los  $\alpha,\beta$ -insaturados.



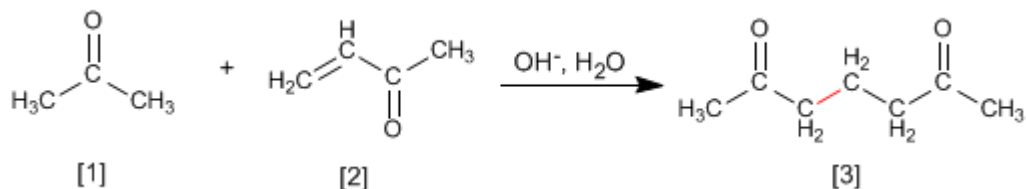
El mecanismo de la reacción comienza con el ataque nucleófilo del cuprato sobre el carbono  $\beta$ , formando un enolato, que se protona en la segunda etapa para dar un enol. El enol tautomeriza a cetona generando el producto final.



- [1] Adición nucleófila del cuprato.
- [2] Protonación del enolato
- [3] Tautomería ceto-enol

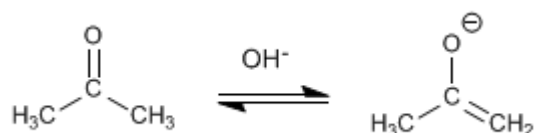
## Adición de Michael y anelación de Robinson

Los enolatos de aldehídos o cetonas se adicionan a los  $\alpha,\beta$ -insaturados para formar 1,5-dicarbonilos. Esta reacción se denomina adición de Michael.

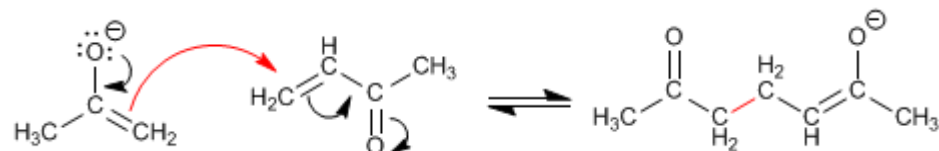


La propanona [1] reacciona con el  $\alpha,\beta$ -insaturado [2] para formar el 1,5-dicarbonilo [3]  
Mecanismo de la Adición de Michael:

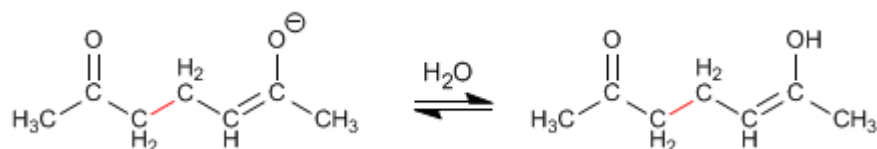
**Etapla 1.** Formación del enolato.



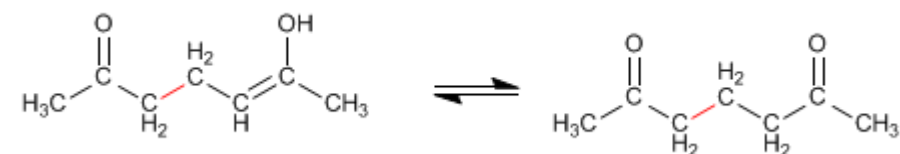
**Etapla 2.** Ataque nucleófilo del enolato al carbono  $\beta$  del  $\alpha,\beta$ -insaturado.



**Etapla 3.** Equilibrio ácido-base



**Etapla 4.** Tautomería ceto-enol

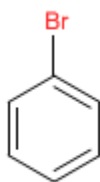


El producto de Michael puede condensar mediante una aldólica intramolecular, formando un  $\alpha,\beta$ -insaturado. El conjunto de la adición de Michael y la aldólica final se conoce como reacción de Robinson

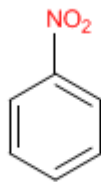
# TEORÍA DEL BENCENO

## Nomenclatura del Benceno

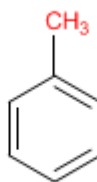
Los bencenos monosustituídos se nombran terminando el nombre del sustituyente en benceno.



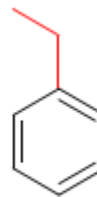
Bromobenceno



Nitrobenceno

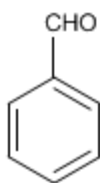


Metilbenceno

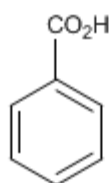


Etilbenceno

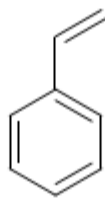
Algunos derivados monosustituídos del benceno tienen nombres comunes ampliamente aceptados.



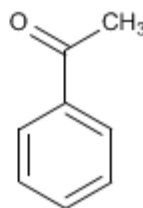
Benzaldehído



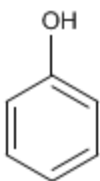
Ácido benzoico



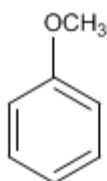
Estireno



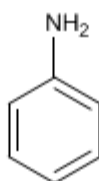
Acetofenona



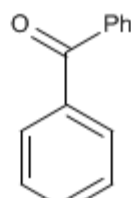
Fenol



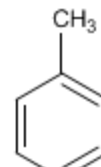
Anisol



Anilina

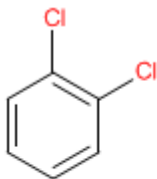


Benzofenona

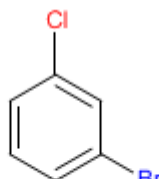


Tolueno

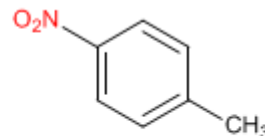
En bencenos disustituídos se emplean los prefijos *orto* (benceno 1,2-disustituído), *meta* (benceno 1,3-disustituído) y *para* (benceno 1,4-disustituído) para indicar la posición de los sustituyentes en el anillo.



o-Diclorobenceno  
(1,2-Diclorobenceno)



m-Bromoclorobenceno  
(1-Bromo-3-clorobenceno)

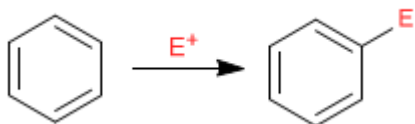


p-Nitrotolueno  
(4-Nitrotolueno)

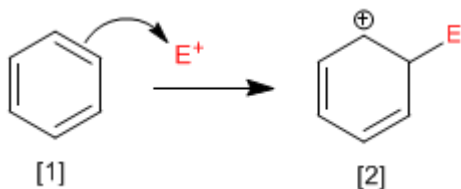


## Sustitución Electrónica Aromática

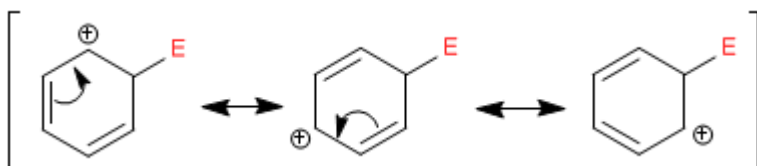
El benceno actúa como nucleófilo, atacando a un número importante y variado de electrófilos.



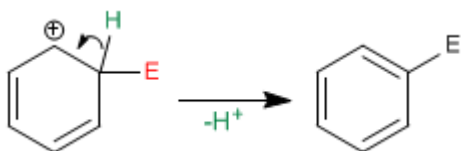
**Etapas 1.** En la primera etapa de la reacción el electrófilo acepta un par de electrones procedentes de la nube  $\pi$  del benceno, formándose un carbocatión estabilizado por resonancia.



El catión ciclohexadienilo [2] deslocaliza la carga positiva según las siguientes estructuras:

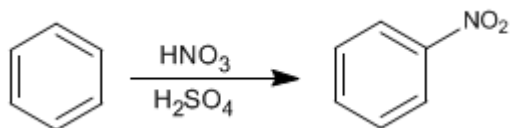


**Etapas 2.** En la segunda etapa el benceno recupera su aromaticidad por pérdida de un protón. Es una etapa rápida conocida como rearomatización del anillo.

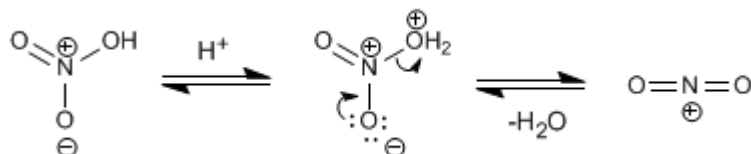


## Nitración del Benceno

El benceno reacciona con la mezcla nítrico-sulfúrica adicionando grupos nitro.

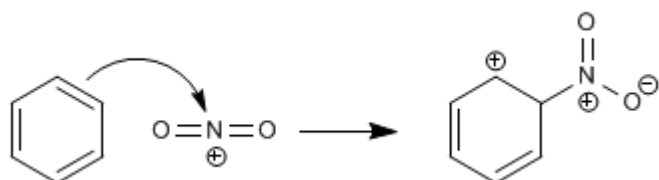


El electrófilo de esta reacción es el catión nitronio,  $\text{NO}_2^+$ . Las concentraciones de este catión en el ácido nítrico son muy bajas para nitrar el benceno, por ello es necesario añadir ácido sulfúrico.

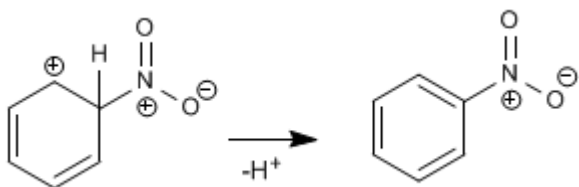


**Mecanismo para la nitración del benceno:**

**Etapla 1.** Ataque del benceno al catión nitronio

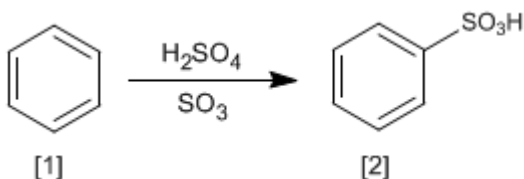


**Etapla 2.** Recuperación de la aromaticidad por pérdida de un protón



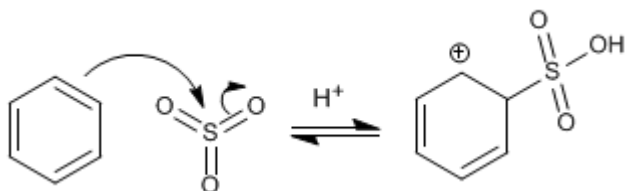
## Sulfonación del Benceno

La reacción del benceno [1] con una disolución de trióxido de azufre en ácido sulfúrico produce ácidos bencenosulfónicos [2].

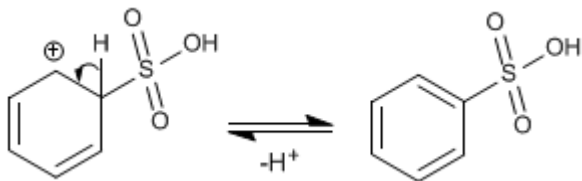


El mecanismo de la sulfonación tiene lugar con las siguientes etapas:

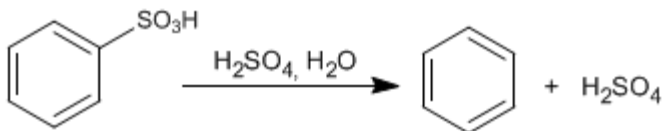
**Etapas 1.** Ataque del benceno al trióxido de azufre



**Etapas 2.** Recuperación de la aromaticidad por pérdida de un protón.

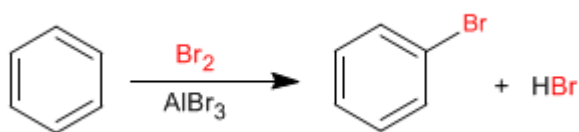


El mecanismo de la sulfonación es reversible, lo cual permite eliminar el grupo  $-\text{SO}_3\text{H}$  por tratamiento con sulfúrico acuoso. Esta propiedad es utilizada para proteger posiciones del benceno, ocupándolas con el grupo  $-\text{SO}_3\text{H}$ .



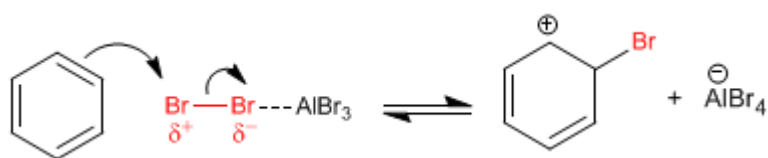
## Halogenación del Benceno

El benceno reacciona con halógenos en presencia de ácidos de Lewis para formar derivados halogenados.

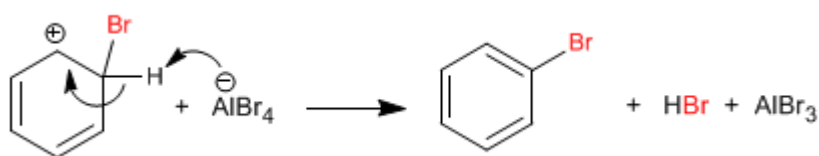


El mecanismo de la halogenación tiene lugar con las siguientes etapas:

**Etapas 1.** La molécula de bromo se polariza al interactuar con el ácido de Lewis. El benceno ataca al bromo polarizado positivamente para formar el catión ciclohexadienilo.



**Etapas 2.** Recuperación de la aromaticidad por pérdida de un protón.

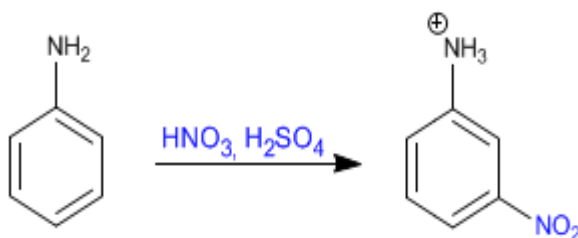


La cloración se puede llevar a cabo de forma similar a la bromación. La reacción con flúor y yodo se realiza muy poco frecuentemente. En el caso del flúor la reacción es difícil de controlar por su elevada reactividad. Por el contrario, el yodo reacciona lentamente y tiene un equilibrio desfavorable.

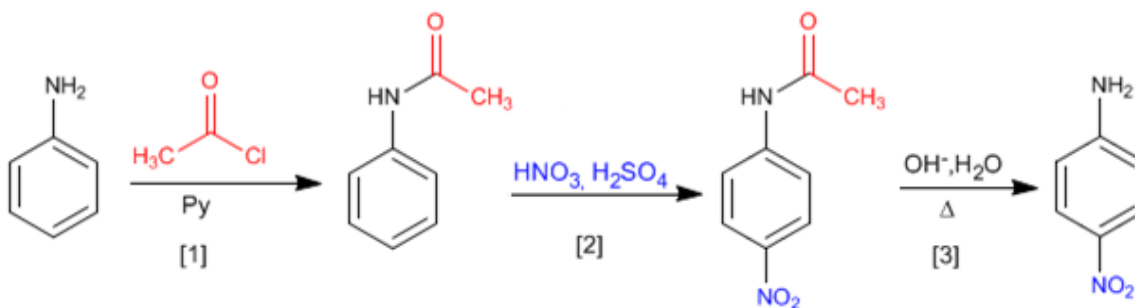
## Benceno - Protección y desprotección del grupo amino

El grupo amino es un activante fuerte, que orienta a orto/para. Sin embargo, en medios ácidos se protona transformándose en un desactivante fuerte (sal de amonio) que orienta a posición meta. Se puede evitar la protonación del amino protegiéndolo con cloruro de etanoilo en piridina.

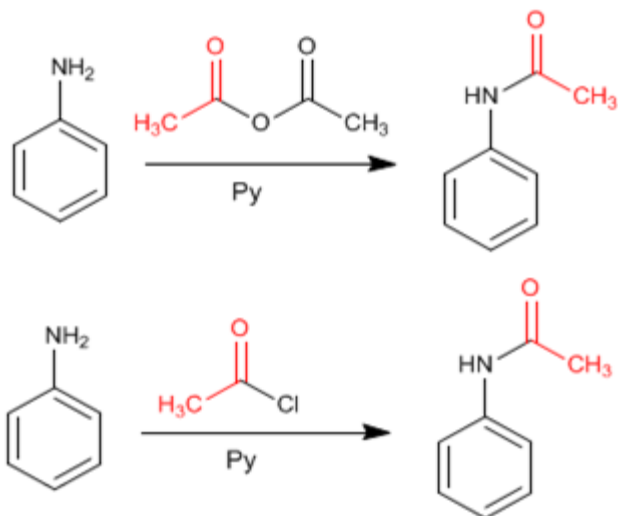
Nitración de la anilina sin protección del amino



Nitración de la anilina con protección del grupo amino, empleando cloruro de etanoilo

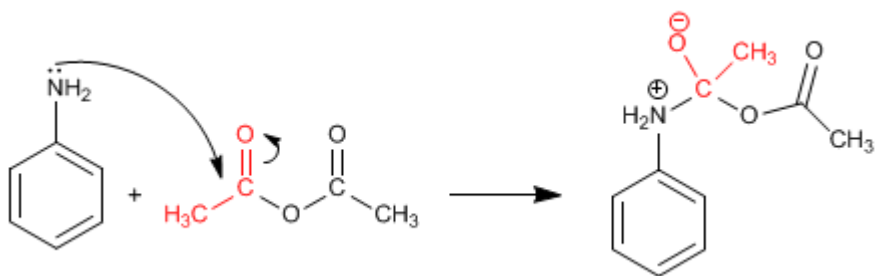


La protección del amino puede realizarse con anhídrido etanoico en piridina, o con cloruro de etanoilo en piridina

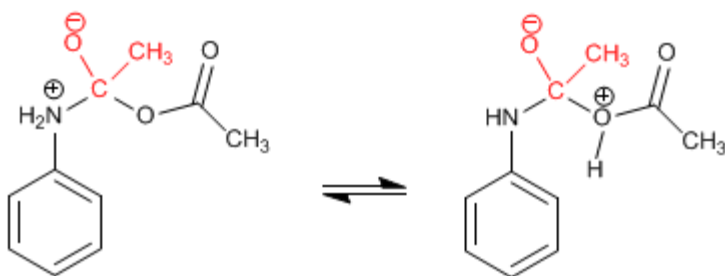


El producto final es una amida, mucho menos básica que la amina de partida y con menos tendencia a protonarse. El mecanismo de la reacción es el siguiente:

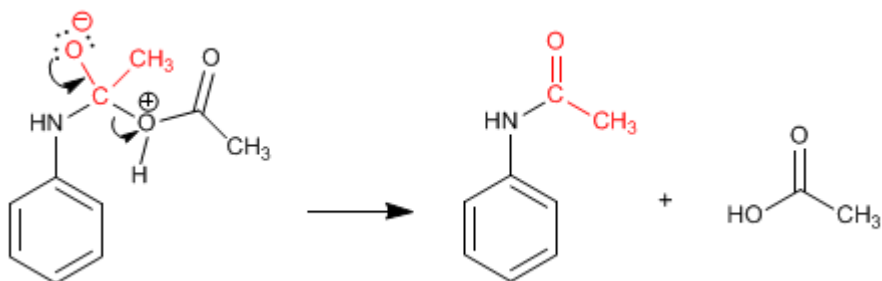
### Etapla 1. Adición



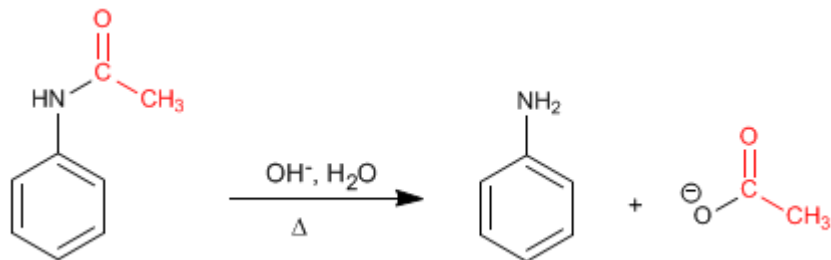
### Etapla 2. Equilibrio ácido-base



### Etapla 3. Eliminación

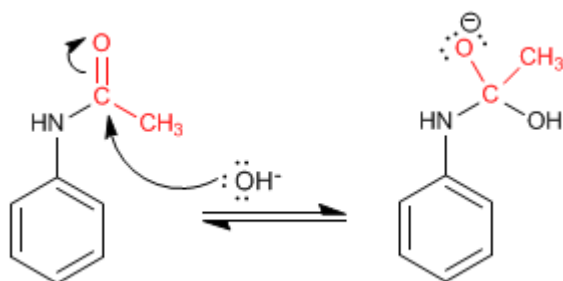


La amida formada se desprotege por hidrólisis ácida o básica, dejando libre la anilina.

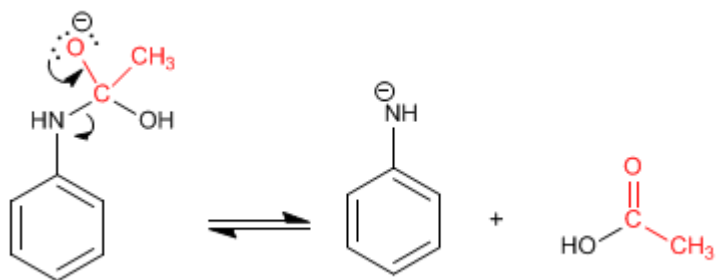


Mecanismo de desprotección en medio básico.

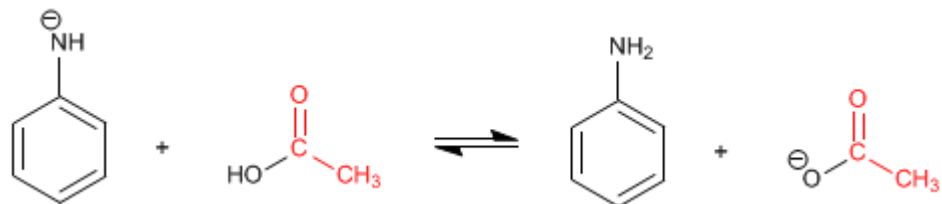
**Etapas 1.** Adición del grupo hidroxilo a la amida



**Etapas 2.** Eliminación

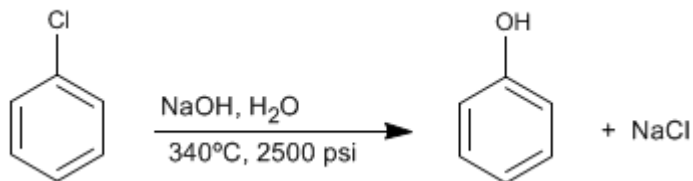


**Etapas 3.** Equilibrio ácido-base



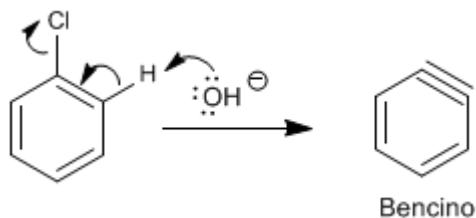
## Sustitución nucleófila aromática: Bencino

Los bencenos halogenados reaccionan con sosa diluida en condiciones de alta presión y temperatura, para formar fenoles. Esta reacción no requiere grupos desactivantes en posición orto/para y sigue un mecanismo diferente al de la sustitución nucleófila aromática por adición-eliminación.

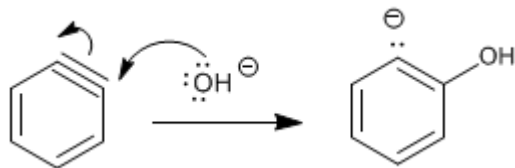


Esta reacción fue descubierta en 1928 por los químicos de la compañía Dow Chemical. El mecanismo consiste en la eliminación de HCl con formación de un intermedio inestable llamado bencino, el cual es atacado por los iones hidróxido del medio, para formar fenol.

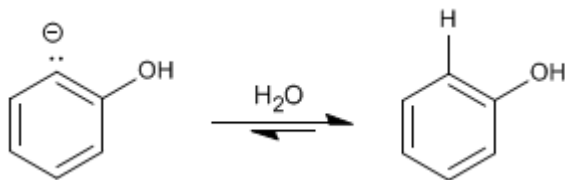
### Etapas 1. Eliminación de HCl



### Etapas 2. Adición del ion hidróxido al bencino



### Etapas 3. Protonación



El mecanismo de esta reacción recibe el nombre de sustitución nucleófila aromática por eliminación-adición.

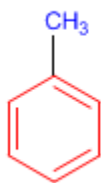
Cuando en el benceno existen sustituyentes produce mezclas, debido al ataque del nucleófilo sobre los dos carbonos del triple enlace.



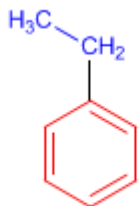
## PROBLEMAS NOMENCLATURA - BENCENO

### Nomenclatura de Benceno - Reglas IUPAC

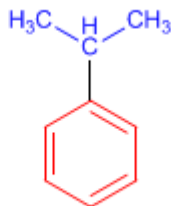
**Regla 1.** En bencenos monosustituídos, se nombra primero el radical y se termina en la palabra benceno.



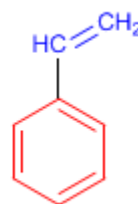
Metilbenceno



Etilbenceno

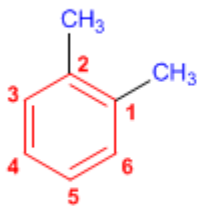


Isopropilbenceno



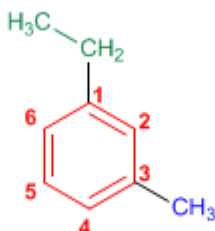
Vinilbenceno

**Regla 2.** En bencenos disustituídos se indica la posición de los radicales mediante los prefijos *orto-* (*o-*), *meta* (*m-*) y *para* (*p-*). También pueden emplearse los localizadores 1,2-, 1,3- y 1,4-.



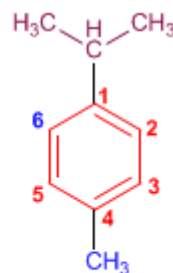
*o*-Dimetilbenceno

(1,2-Dimetilbenceno)



*m*-Etilmetilbenceno

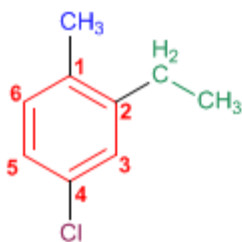
(1-Etil-3-metilbenceno)



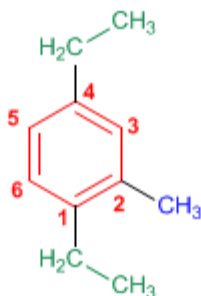
*p*-Isopropilmetilbenceno

(1-Isopropil-4-metilbenceno)

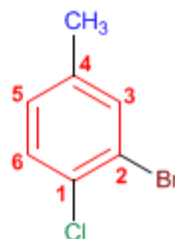
**Regla 3.** En bencenos con más de dos sustituyentes, se numera el anillo de modo que los sustituyentes tomen los menores localizadores. Si varias numeraciones dan los mismos localizadores se da preferencia al orden alfabético.



4-Cloro-2-etil-1-metilbenceno

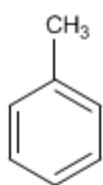


1,4-Dietil-2-metilbenceno

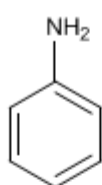


2-Bromo-1-cloro-4-metilbenceno

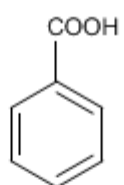
**Regla 4.** Existen numerosos derivados del benceno con nombres comunes que conviene saber:



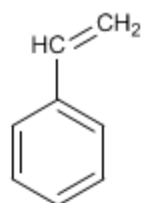
Tolueno



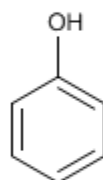
Anilina



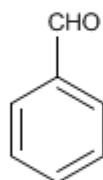
Ac. Benzoico



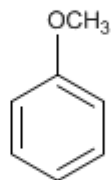
Estireno



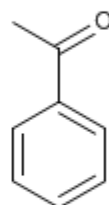
Fenol



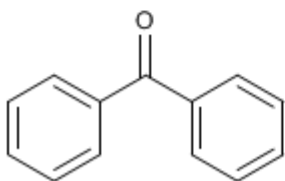
Benzaldehído



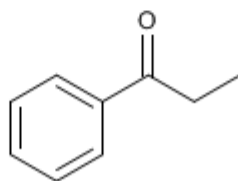
Anisol



Acetofenona



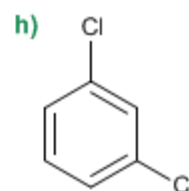
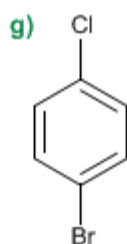
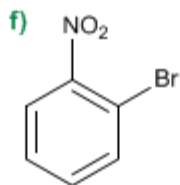
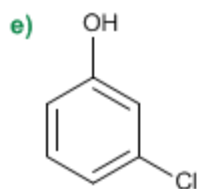
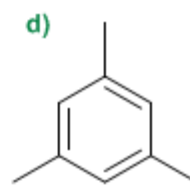
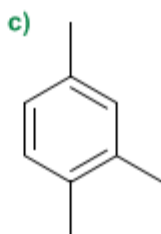
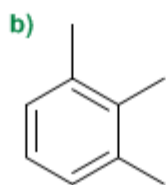
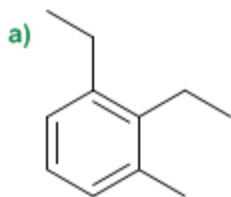
Benzofenona



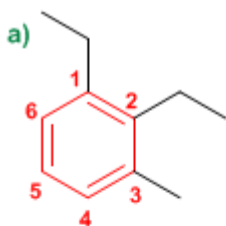
Propiofenona

## Nomenclatura de Benceno - Problema 0.1

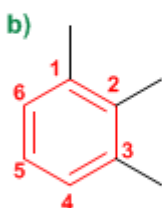
Nombra los siguientes derivados del benceno:



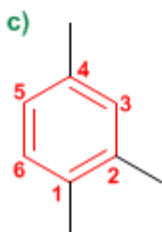
Solución



1. Cadena principal: benceno
2. Numeración: los sustituyentes deben tomar los menores localizadores, y además, se asignan los localizadores menores a los grupos que van antes en el orden alfabético (etilo antes que metilo)
3. Sustituyentes: etilos en 1,2 y metilo en 3.
4. Nombre: 1,2-Dietil-3-metilbenceno



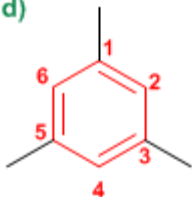
1. Cadena principal: benceno
2. Numeración: los sustituyentes deben tomar los menores localizadores.
3. Sustituyentes: metilos en posición 1,2,3.
4. Nombre: 1,2,3-Trimetilbenceno



1. Cadena principal: benceno
2. Numeración: los sustituyentes deben tomar los menores localizadores.
3. Sustituyentes: metilos en posición 1,2,4.
4. Nombre: 1,2,4-Trimetilbenceno

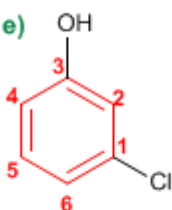
El anillo se numera para que los sustituyentes tomen los localizadores más bajos. En caso de empate se tiene en cuenta el orden alfabético

d)



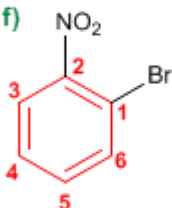
1. Cadena principal: benceno
2. Numeración: se parte de un metilo y se numera en cualquier dirección.
3. Sustituyentes: metilos en 1,3,5.
4. Nombre: 1,3,5-Trimetilbenceno

e)



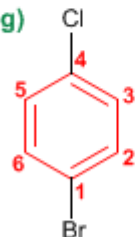
1. Cadena principal: benceno
2. Numeración: la numeración comienza en el cloro (va antes alfabéticamente) y prosigue por el camino más corto hacia el hidroxilo.
3. Sustituyentes: cloro en posición 1 e hidroxilo en posición 3 (posición meta)
4. Nombre: 1-Cloro-3-hidroxibenceno (*m*-Clorohidroxibenceno)

f)



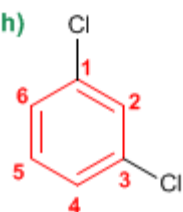
1. Cadena principal: benceno
2. Numeración: la numeración comienza en el bromo (preferencia alfabética)
3. Sustituyentes: bromo en posición 1 y nitro en posición 3 (posición orto)
4. Nombre: 1-Bromo-3-nitrobenzono (*o*-Bromonitrobenzono)

g)



1. Cadena principal: benceno
2. Numeración: comienza en el bromo (preferencia alfabética sobre el cloro)
3. Sustituyentes: bromo en 1 y cloro en 4 (posición para)
4. Nombre: 1-Bromo-4-clorobenceno (*p*-Bromoclorobenceno)

h)



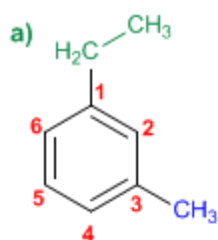
1. Cadena principal: benceno
2. Numeración: localizadores más bajos posibles a los cloros.
3. Sustituyentes: cloros en posición 1,3.
4. Nombre: 1,3-Diclorobenceno (*m*-Diclorobenceno)

## Nomenclatura de Benceno - Problema 0.2

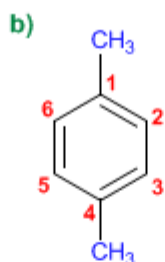
Formular los siguientes derivados del benceno:

- |   |   |
|---|---|
| a) 1-Etil-3-metilbenceno                | k) 4,5-Difenil-1-octeno                       |
| b) <i>p</i> -Dimetilbenceno             | l) 2-Fenil-4-metilhexeno                      |
| c) 1-Butil-3-etilbenceno                | m) 1-(metiletil)-4-(2-metilpropil)benceno     |
| d) <i>o</i> -Cloronitrobenceno          | n) 6-Fenil-3-metilhexa-1,4-dieno              |
| e) <i>m</i> -Bromoclorobenceno          | o) <i>cis</i> -1-Fenil-1-buteno               |
| f) <i>p</i> -Diisopropilbenceno         | p) <i>trans</i> -2-Fenil-2-buteno             |
| g) 1- <i>tert</i> -Butil-4-metilbenceno | q) 7-Etil-4,5-difenildec-5-en-1-ino           |
| h) <i>o</i> -Alilvinilbenceno           | r) <i>m</i> -Diciclohexilbenceno              |
| i) <i>m</i> -Etilpropilbenceno          | s) <i>p</i> -Ciclobutilciclobutilbenceno      |
| j) 2-Etil-1,4-dimetilbenceno            | t) 3-(1,1-Difeniletil)-3-metilhex-1-en-5-ino. |

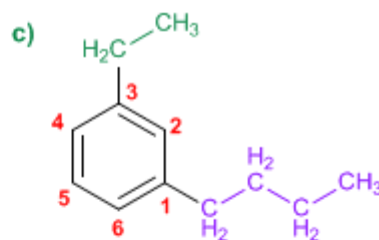
### Solución



1-Etil-3-metilbenceno



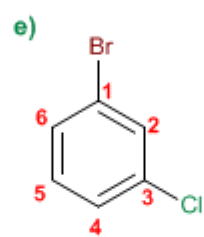
*p*-Dimetilbenceno



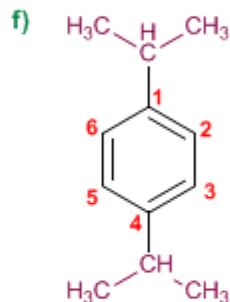
1-Butil-3-etilbenceno



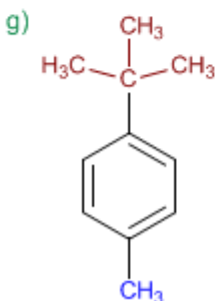
*o*-Cloronitrobenceno



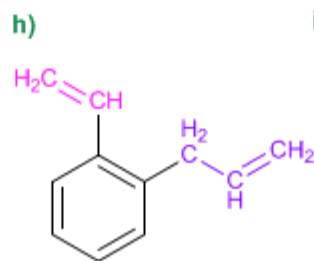
*m*-Bromoclorobenceno



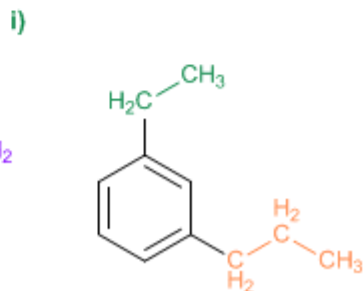
*p*-Diisopropilbenceno



1-*tert*-Butil-4-metilbenceno

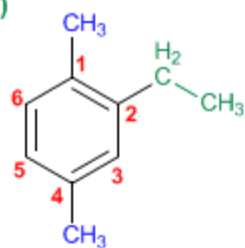


*o*-Alilvinilbenceno



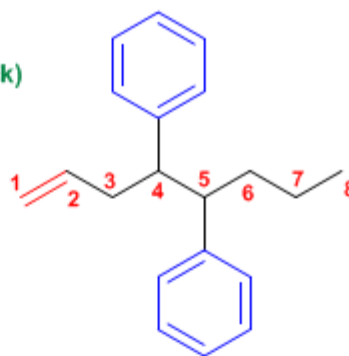
*m*-Etilpropilbenceno

j)



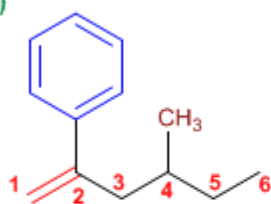
2-Etil-1,4-dimetilbenceno

k)



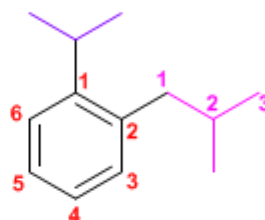
4,5-Difenil oct-1-eno

l)



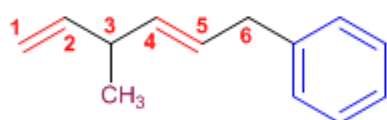
2-Fenil-4-metilhex-1-eno

m)



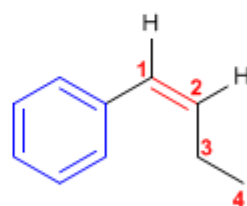
1-(metiletil)-2-(2-metilpropil)benceno

n)



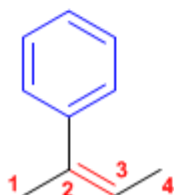
6-Fenil-3-metilhexa-1,4-dieno

o)



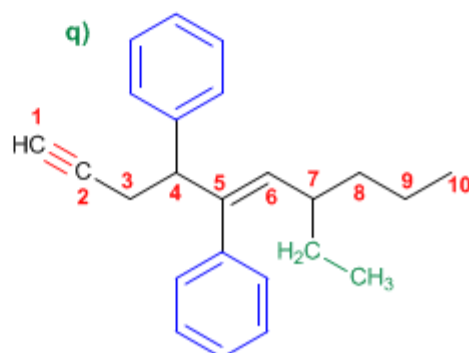
cis-1-Fenil-1-butenó

p)



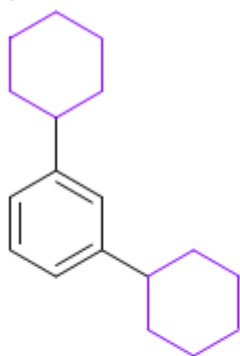
trans-2-Fenil-2-butenó

q)



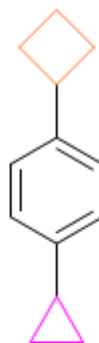
7-Etil-4,5-difenildec-5-en-1-ino

r)



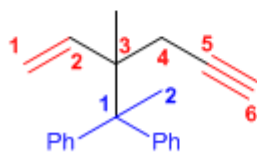
*m*-Diciclohexilbenceno

s)



*p*-Ciclobutilciclopropilbenceno

t)



3-(1,1-Difeniletil)-3-metilhex-1-en-5-ino.

## *Agradecimientos:*

❖ <http://www.quimicaorganica.org>

❖ <http://www.taringa.net/perfil/jose07070012>